

The key factors affecting cumulative live birth rate after single oocyte retrieved in women during IVF/ICSI-ET: a retrospective analysis of 1380 PCOS patients

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Research Article

Keywords: Cumulative live birth, single oocytes retrieved, PCOS, Cox proportional risk regression model.

Posted Date: March 12th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-253430/v1>

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Abstract

Background: The factors affecting the cumulative live birth rate (CLBR) of PCOS patients who received in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) are unknown.

Methods: Here we carried out a retrospective analysis of 1380 PCOS patients who received IVF/ICSI-ET for the first time from January 2014 to December 2016. According to the cumulative live births of PCOS patients after single oocyte collection, they were divided into cumulative live births group (group A) and non-cumulative live births group (group B).

Results: The conservative cumulative live birth rate was 63.48%. There were 876 cumulative live births (group A) and 504 non-cumulative live births (group B) according to whether the patients had live births or not. Competition analysis showed that duration of infertility, primary/secondary type of infertility, stimulation protocols, starting dose of gonadotrophins and oocyte retrieved numbers were significantly correlated with CLBR. The Cox proportional risk regression model of PCOS patients showed that stimulation protocols had a significant impact on CLBR. Patients in the GnRH-antagonist protocol group and the mild stimulation protocol had lower CLBR than those in the Prolonged GnRH-agonist protocol, which was statistically significant. PCOS patients with the starting dose of gonadotrophins greater than 112.5u had lower CLBR than those with less than 100u, which was statistically significant. Women with 11-15 oocytes and 16-20 oocytes had higher CLBR than women with 1-9 oocytes, which was statistically significant.

Conclusions: According to our statistical results, patients with PCOS represent a challenge for reproductive medicine.

Background

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women, which affects 10% reproductive age women[1]. Patients with PCOS were often treated with in vitro fertilization (IVF) or intracytoplasmic sperm microinjection (ICSI) when multiple ovulation-induced infertility[2]. However, during the process of IVF/ICSI treatment, PCOS patients often suffered from overweight or obesity, hormone metabolism or Insulin resistance(IR), and other endocrine and metabolic abnormalities, which may affect the quality of oocyte, early embryo development and endometrial receptivity[3]. Therefore, the basic information of PCOS patients (age, body mass index (BMI), number of antral follicles (AFC), infertility duration, primary/secondary infertility type and basic hormone level, etc.) and clinical treatments (treatment protocols, use of gonadotropin, sex hormone level on HCG trigger day, endometrial thickness on HCG trigger day, oocyte retrieved numbers and insemination method, etc.) significantly affect the outcome of IVF/ICSI. For example, women under the age of 35 have a higher live rate than women over the age of 35 in IVF-ET treatment[4], women with BMI higher than 28kg / m² had lower live birth rate[5], moreover, treatment protocols and the use of gonadotropin also affected the living rate of patients[6-8], and the patients with 6-15 oocytes retrieved numbers had the highest live rate and the least

complications[9] . Although most of researchers have focused on this issue, the related key factors are still unclear[6, 8, 10, 11] . Therefore, we designed this study to analyze the data of PCOS patients after IVF/ICSI-ET, in order to find the related key factors affecting the results of IVF/ICSI-ET in PCOS patients. Generally, PCOS patients are usually suggested to freeze all embryo in order to avoid the occurrence of moderate and severe OHSS. Thus, We chose the cumulative pregnancy rate (CLBR) as the final evaluation index, which is the total live rate of fresh and thawing cycles after single oocytes collection[12, 13] . In our study, we retrospectively analyzed the clinical data of PCOS patients, and divided them into cumulative live birth group (group A) and non-cumulative live birth group (group B) according to whether there were live births. The differences between the two groups in general characteristics and clinical treatment data were statistically analyzed. The competitive risk model was used to analyze the single factor of CLBR, and Cox proportional risk regression model was used to evaluate which factors had more influence on CLBR.

Materials And Methods

Patients Selection

This study was a retrospective analysis of PCOS patients who received in IVF/ICSI for the first time from January 2014 to December 2016 at the Reproductive Medicine Center of Jiangxi Maternal and Child Health Hospital, P.R. China. The data of fresh and thawed transplantation cycles after single oocyte retrieved were collected and were followed for 2-4 years until December 2018. PCOS patients were diagnosed based on the Rotterdam criteria[14], including oligoovulation or anovulation and polycystic ovary (PCO). Exclusion criteria included unilateral ovariectomy, recurrent spontaneous abortion (defined as the loss of three previous spontaneous pregnancies), congenital or acquired uterine malformations, abnormal karyotype analysis, and the exclusion of endometriosis, uterine fibroids, adenomyosis, severe hyperprolactinemia and thyroid disease history. At the same time, we also excluded the cycles in which live births have not yet been obtained but have frozen embryos remaining, and clinical pregnancies that have not yet been delivered. According to the cumulative live births of PCOS patients after single oocyte collection, they were divided into cumulative live births group (group A) and non-cumulative live births group (group B).

Blood sampling and sex hormone measurement

Blood samples were collected on the third day of the menstrual cycle and on the day of HCG injection. The serum was used for the quantitative determination of sex hormone (follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E_2), prolactin (PRL) and testosterone (TES)) level by chemiluminescent enzyme immunoassay using Automated Enzyme Immunoassay Analyzer (AIA-2000ST, TOSOH CORPORATION).

Treatment protocols and Transplantation

Prolonged GnRH-agonist protocol

GnRH-a (3.75mg) was used in the second or three day of menstrual cycle in prolonged GnRH-agonist protocol. Gonadotrophin stimulation were started after 28 or 38 days following the criteria: no ovarian cysts > 8mm, E₂ < 50pg/ml, FSH < 5 u/L, LH < 5 u/L. Initial, patients received 75-150u/d of gonadotrophins according to the patient's age, BMI, serum basal FSH levels, LH levels, E₂ levels and antral follicle count.

GnRH-agonist protocol

All subjects received oral contraceptive pills (OCP) for 21 days starting on menstrual day 5 in the cycle prior to the treatment cycle in GnRH-agonist protocol. Subcutaneous injection of triptorelin 0.1 mg was given on day 21 of OCP administration and continued until the triggering day. gonadotrophins injection with a dose of 75-150 u daily was started on the next menstrual on day 3.

GnRH-antagonist protocol

On day 2 or 3 of the menstrual cycle, when the follicular diameter of the patients was less than 8 mm and the blood E₂ was less than 50 pg / ml, gonadotrophins injection with a dose of 75-150u daily was started. When the dominant follicle reached a diameter of 12 mm or the level of estradiol were >200 pg/mL, GnRH antagonist 0.25 mg was given daily afterwards. Treatment with antagonist and gonadotrophins was continued until the triggering day.

Mild Stimulation protocol

Oral administration of letrozole 2.5mg/d or clomiphene 50mg/d on the third day of menstruation, and fifth days of intramuscular injection of gonadotrophins 75-150u/d, according to the growth of follicles, adjust the dose of gonadotrophins to trigger day.

Oocyte collection and zygote scoring

The time and dose of gonadotrophins were adjusted according to ovarian response as monitored by serum E₂ levels and vaginal ultrasound. When the dominant follicle was ≥ 19 mm in diameter or at least 3 follicles were ≥ 17.5 mm in diameter and 1/3 follicles larger than 1.4 cm, recombinant human FSH was stopped, and a single injection of 250ug of HCG (Merck-Serono, Darm-stadt, Germany) was administered in the Prolonged GnRH-agonist protocol, GnRH-agonist protocol and GnRH-antagonist protocol. According to E₂ value, HCG 1000u - 2000u (1000 u/branch, China Li Zhu company) was added. After 36-38 hours, the oocytes were taken by transvaginal ultrasound-guided transvaginal puncture. One or two embryos were transferred 3-5 days after oocytes collection under the guidance of abdominal B-ultrasound. GnRH-a 0.1 mg and HCG 2000u were injected intramuscularly that night in the mild stimulation protocol. After 34-36 hours, the oocytes were removed by operation. If the patient used the mild stimulation protocol, moderate to severe ovarian hyperstimulation syndrome (OHSS) might occur, P level is higher or other situation which were not suitable for transplantation, the transplantation is cancelled and all embryos are frozen after informed consent of both the patient and his wife.

The planned transplant patients received intramuscular injection of progesterone 80 mg daily from the day of operation. After transplantation, they were given intramuscular injection of progesterone 60mg/d or modified progesterone vaginal agglomerate (Orenorone, Merck) for vaginal delivery, plus Dydrogesterone tablets (Duphaston, 10 mg / tablets, Solvay pharmaceutical) oral administration, bid. Four weeks later, the clinical pregnancy was confirmed by ultrasound. After the occurrence of fetal heart rate, the luteal support drug gradually decreased.

Freeze-thaw embryo transfer

Thawed embryo transfer will be carried out in patients with fresh cycle whole embryo cryopreservation or patients with previous embryo cryopreservation without live birth at an optional time. The hormone replacement cycle begins on the 2 - 4 day of menstrual cycle, oral Estradiol valerate tablets (1 mg / tablets, German Bayer medical care) 4 - 8 mg/d. The endometrial thickness is monitored by B-mode ultrasound, and the dosage is increased according to the endometrial thickness. When the thickness of endometrium was ≥ 7 mm after 12-16 days, progesterone injection was added for 80 mg/d. Cleavage embryo or blastocyst transfer at 4 or 6 days after injection.

Live birth is defined as the newborns with over 28 weeks of gestation and one of the four vital signs of heartbeat, respiration, umbilical cord pulsation and voluntary muscle contraction after delivery. The cumulative live birth rate is the total probability that the total live birth rate after transferring all the embryos which are from one oocyte retrieved, excluding those who have not yet obtained a live birth and still have frozen embryos, as well as those who have received clinical pregnancy but have not yet obtained a live birth.

Statistical Analysis

The characteristics of the live birth patients (group A) and no live birth patients (group B) were compared. For continuous variables, Student's t-test was used for data with homogeneous variance and the Chi-square tests were applied to detect differences between categorical variables. The P-values correspond to tests for difference between the two groups with a significance level of 5%. Data are presented as mean (SD) or number (%) as relevant. The CLBRs were compared by Gray's test using a competing risk analysis. Cox proportional hazard model was used to evaluate the relative prognostic significance of female age, duration of infertility, type of infertility, treatment protocols, starting dose of gonadotrophins and oocyte retrieved in relation to CLBR. Interactions between the independent covariates were tested. For age, subjects were categorized into four age groups (<30, 30–34, 35-38 and >38 years). They were divided into three group (<2, 3–4 and >4 years) according to the years of infertility. They are divided into 3 groups (<100u, 100u–112.5u and >112.5u) based on the starting dose of gonadotrophins. The four groups for the number of retrieved oocytes were 1–10, 11–15, 16–20 and >20. All analyses were conducted using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics

We enrolled 1380 PCOS patients who underwent first oocyte retrieved. The birth outcomes were followed up for 2-4 years, including fresh and thawed cycles. The conservative cumulative live birth rate was 63.48%. There were 876 cumulative live births (group A) and 504 non-cumulative live births (group B) according to whether the patients had live births or not. Among them, there were 1087 Prolonged GnRH-agonist protocol, 222 GnRH-agonist protocol, 57 GnRH-antagonist protocol and 14 mild stimulation protocol.

As shown in table 1, the distribution of infertility years in group A was significantly different from that in group B. The number and proportion of patients with infertility more than 4 years in the two groups were 298 (35.27%) and 206 (41.78%), respectively. The proportion of primary infertility and secondary infertility in group A was significantly different from that in group B. The number and corresponding proportion of patients with primary infertility in the two groups were 620 (70.78%) and 329 (65.28%). There was no statistical difference in the results of basic sex hormones levels (FSH, LH, E₂, PRL, T), age distribution, BMI and AFC values between the two groups.

Clinical Outcomes

In the treatment plan comparison (Table 2), the treatment plan distribution of group A and the ratio of group B were statistically significant; the number and proportion of Prolonged GnRH-agonist protocol cases in the two groups were 729 (83.22%) and 358 (71.03%), respectively. The number and proportion of 112.5u dose groups in the two groups were 398 (45.43%) and 203 (40.28%), respectively. The proportion of 11-15 oocytes and 16-20 oocytes in group A was higher than that in group B (258, 29.45% and 110, 21.83%; 243, 27.74% and 122, 24.21%), respectively. The number of available embryos in group A was higher than that in group B (4.81 ± 2.91 and 3.41 ± 2.69). There was no statistical difference in total gonadotrophins, total days of gonadotrophins, LH, P, E₂ and endometrial thickness between the two groups on HCG day. Furthermore, no statistical difference was found in the proportion of fertilization methods and the number of embryo transfer between the two groups.

Gray's Test

Competition analysis showed that duration of infertility, primary/secondary type of infertility, stimulation protocols, starting dose of gonadotrophins and oocyte retrieved numbers were correlated with CLBR, and the difference was statistically significant (Figure 1-7). The older the female is, the higher the CLBR tends to be, but the difference is not statistically significant (Figure 2).

Cox proportional risk regression model analysis

The Cox proportional risk regression model of PCOS patients showed that stimulation protocols had a significant impact on CLBR (Table 3). Women in the GnRH-antagonist protocol group and the mild stimulation protocol had lower CLBR than those in the Prolonged GnRH-agonist protocol (adjusted risk

ratio (aHR): 0.71; 95% CI: 0.48-1.06; P = 0.0094 and aHR: 0.4; 95% CI: 0.15-1.08; P = 0.0001), which was statistically significant. PCOS patients with the starting dose of gonadotrophins greater than 112.5u had lower CLBR than those with less than 100u (aHR: 0.9; 95% CI: 0.64-1.27; P = 0.0358), which was statistically significant. There was a higher CLBR in women with the starting dose of gonadotrophins of 100u or 112.5u than in women with the starting dose of gonadotrophins of less than 100u, but there was no statistical significance. Women with 11-15 oocytes and 16-20 oocytes had higher CLBR than women with 1-9 oocytes (AHR: 1.54; 95% CI: 1.25-1.89; P < 0.0001 and AHR: 1.28; 95% CI: 1.04-1.58; P = 0.02), which was statistically significant. There was no significant difference in female age, duration of infertility and primary/secondary types of infertility in the model, but CLBR increased with the increase of female age and duration of infertility.

Discussions

Since 1984, the first live birth of thawed frozen embryo—the number of thawed frozen embryo transfer and the related pregnancy rate are increased with the development of new technology[15]. This practice is encouraged by the strategy of single embryo transfer and the prevention of moderate to severe OHSS in high-risk women[16]. Correspondingly, single cycle live birth rate alone is not enough to evaluate the IVF success rate of patients. CLBR emerged as a method to summarize the IVF success rate of fresh and frozen embryo transfer[17]. PCOS patients, as a representative of high reactive population prone to OHSS, are not enough to report the success rate of IVF only based on the results of fresh embryo transfer. The report should not only include the results related to fresh embryo transfer, but also include the results of frozen thawed embryo, so as to provide a comprehensive success rate[12]. Therefore, CLBR is of great significance for the prognosis of patients with PCOS undergoing IVF / ICSI-ET.

In our retrospective single-center data analysis, we included 1380 PCOS patients who underwent first oocyte retrieved. The birth outcomes were followed up for 2–4 years, including fresh and thawed cycles. The conservative cumulative live birth rate was 63.48%. In the data analysis of the cumulative live birth group (A group) and the non-cumulative live birth group (B group), we found that the following two groups of data were statistically significant difference: duration of infertility, primary/secondary type of infertility, stimulation protocols, starting dose of gonadotrophins, oocyte retrieved and the number of embryos available. Taking these factors and female age into Cox proportional risk regression model, we found that the stimulation protocols, starting dose of gonadotrophins and oocyte retrieved had significant effects on CLBR.

Stimulation protocols greatly affects the oocyte, embryo and endometrium of PCOS patients, thus affecting the success rate of IVF treatment. In our study, women in the GnRH-antagonist protocol group and the mild stimulation protocol had lower CLBR than those in the Prolonged GnRH-agonist protocol, which was statistically significant. PCOS patients have a variety of ovulation induction therapies, including four in our study: Prolonged GnRH-agonist protocol, GnRH-agonist protocol, GnRH-antagonist protocol and mild stimulation protocol. Standard GnRH-agonist protocol is the classical protocol, which is most widely used in the early IVF-ET treatment of PCOS patients[18]. Prolonged GnRH-agonist protocol,

GnRH-antagonist protocol and mild stimulation protocol are all based on the comparison of this stimulation protocol. Compared with the standard GnRH-agonist protocol, prolonged GnRH-agonist protocol increased the down-regulation time, mostly used in IVF-ET treatment of endometriosis[19]. In PCOS treatment, the prolonged GnRH-agonist protocol increased the endometrial receptivity by prolonging the down regulating time, thus increasing the implantation rate and pregnancy rate, but did not increase the incidence of OHSS[20]. In the meanwhile, although the GnRH-antagonist protocol has a lower rate of OHSS, it often shows a lower pregnancy rate[21]. PCOS patients treatment with mild stimulation protocol were similar to antagonist program, whom did not undergo down-regulation, and had low dose of drugs to promote ovulation with or without antagonists. Compared with standard GnRH-agonist protocol, it related to lower OHSS rate, but had higher cycle cancellation rate. CLBR after repeated ovulation was not affected, and was mostly used for the decline of ovarian function[22–24]. In summary, the Prolonged GnRH-agonist protocol improves the CLBR of single oocyte collection in PCOS patients, and is the recommended scheme for IVF treatment in PCOS patients.

Because of the abnormal endocrine level, PCOS patients are often accompanied by increased androgen level, abnormal glucose tolerance and insulin resistance[25]. In Barber's study, the two groups of PCOS patients were slow in response to IVF treatment, with abnormal follicular development, which easily led to OHSS[26]. In order to reduce the occurrence of OHSS, the starting dose of gonadotrophins in PCOS patients is very important. The low dose FSH stimulation strategy is recommended[7, 8]. The dosage of commonly used ovulation promotion drugs starts from 75-112.5u. Our statistics also confirm that PCOS patients with the starting dose of gonadotrophins greater than 112.5u had lower CLBR than those with less than 100u. However, although there was no statistical significance, women with the starting dose of gonadotrophins of 100u or 112.5u had higher CLBR than those with less than 100u. These could be contributed to: 1) outcome parameters are rising with the extent of the reaction to gonadotrophins stimulation, coming to a plateau and decreasing with stronger response to stimulation. 2) Lower doses of gonadotrophins leads to smaller reactions, which would be in favor of more sensitive patients like those with PCOS[7].

A recent clinical randomized controlled study, which was a comparison of the outcomes of GnRH-antagonist and GnRH-agonist protocols in no PCOS patients, showed that the number of Oocyte retrieved had a significant effect on CLBR in both protocols. Furthermore, the lowest CLBR was found in 1–3 oocytes retrieved subgroups, and the highest CLBR was found in > 15 oocytes retrieved subgroups; but no significant difference was found when comparing the CLBR in each oocyte retrieved subgroups between GnRH-antagonist and GnRH-agonist protocols. These results indicated that the effect of the number of oocytes retrieved on CLBR was not affected by different protocols[27]. In other studies, some researchers also observed that the optimal number of oocytes retrieved for good CLBR and avoiding severe OHSS was 6–15 in the GnRH-antagonist protocols of non PCOS patients[9]. However, the ideal number of oocytes retrieved was 10–14 in another study of women aged 35–40[28]. At the same time, there was a significant positive correlation between the number of oocytes retrieved and CLBR in a retrospective analysis of IVF-ET treatment in PCOS patients. In addition, though retrieving more than 10 oocytes leads to no significant benefit to CLBR but generates surplus embryos[11]. In these studies, we found that

women with PCOS who had 11–15 and 16–20 oocytes retrieved subgroups had higher CLBR than women with 1–9 in IVF-ET treatment, similar to previous studies. Therefore, we speculated that the high reactivity could be the key factor leading to a slightly higher optimal number of oocytes retrieved in PCOS patients.

Conclusion

Patients with PCOS represent a challenge for reproductive medicine. According to our statistical results, the CLBR of PCOS patients increased significantly after a single oocyte collection when we used Prolonged GnRH-agonist protocol, when the first starting dose of gonadotrophins was 100u-112.5u and when the number of oocytes obtained was 11–20.

Declarations

Ethics approval and consent to participate

The patient signed a written informed consent form prior to recruitment. This study is in line with the Helsinki Declaration and approved by the Ethics Review Body Committee of the Jiangxi Maternal and Child Health Hospital.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files]

Competing interests of interest

None of the authors declared a conflict of interest of any kind.

Funding

This work was supported by National Natural Science Foundation of China (No. 81960288) to Q.F.W, (No. 81960271) to J.T and (No.81802621) to Z.Y.Z.

Authors' contributions

Q.F.W., Z.Y.Z and Y.L were responsible for conception and design of study. Y.L and J.T were responsible for drafting the manuscript, Y.L and L.Z.X were responsible for analyzing and interpreting the data.

Acknowledgements

We thank the staff at Reproductive Medicine Center of Jiangxi Maternal and Child Health Hospital for helping us collect clinical data.

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Tables

Table 1 Patient characteristics between two groups

Characteristics	NO Live Birth	Live Birth	t/ χ^2	p
Numbers of cycle	504	876		
AGE (Years)				
<30	368(73.02%)	679(77.51%)		
30-34	113(22.42%)	173(19.75%)		
35-38	19(3.77%)	21(2.4%)		
>38	4(0.79%)	3(0.34%)	5.3176	0.15
BMI (Kg/m ²)	23.28±3.53	22.96±3.48	1.67	0.0955
AFC	22.28±4.57	22.57±5.1	0.91	0.3651
Duration of Infertility (Years)				
0 ~ 2	99(20.08%)	204(24.14%)		
3 ~ 4	188(38.13%)	343(40.59%)		
>4	206(41.78%)	298(35.27%)	6.2535	0.0439
Type of Infertility				
Primary Infertility	329(65.28%)	620(70.78%)		
Secondary Infertility	175(34.72%)	256(29.22%)	4.5036	0.0338
bFSH	5.7±1.46	5.85±1.56	1.64	0.102
bE2	48.51±93.96	52.27±156.89	0.54	0.5913
bPRL	16.5±19.43	15.68±8.81	0.85	0.3951
bLH	9.39±5.88	9.82±7.18	1.17	0.2411
bT	44.38±17.69	43.48±18.44	0.84	0.4032

Table 2 Clinical treatment between two groups

Characteristic	NO Live Birth	Live Birth	t/ χ^2	p
Numbers of cycle	504	876		
Treatment Protocols				
Prolonged GnRH-agonist	358(71.03%)	729(83.22%)		
GnRH-agonist	109(21.63%)	113(12.9%)		
GnRH-antagonist	28(5.56%)	29(3.31%)		
Mild Stimulation	9(1.79%)	5(0.57%)	29.7399	<.0001
Start Dose of Gonadotrophins (IU)				
<100	50(9.92%)	87(9.93%)		
100	180(35.71%)	324(36.99%)		
112.5	203(40.28%)	398(45.43%)		
>112.5	71(14.09%)	67(7.65%)	15.3588	0.0015
Total Dose of Gonadotrophins (IU)	1934.7±1105.3	1947.13±1007.42	0.21	0.8356
Total days of Gonadotrophins	12.61±3.27	12.95±3.25	1.87	0.0617
LH on HCG trigger day (mIU/mL)	1.43±1.51	1.22±1.18	2.53	0.0116
P on HCG trigger day (ng/mL)	0.69±0.77	0.6±0.81	0.64	0.5201
E2 on HCG trigger day (pg/mL)	3332.21±1922.96	3253.91±1845.03	1.49	0.1397
Endometrial thickness on HCG trigger day (mm)	10.5±2.49	10.69±2.12	1.46	0.1433
Oocytes Retrieved				
1 ~ 10	132(26.19%)	150(17.12%)		
11 ~ 15	110(21.83%)	258(29.45%)		
16 ~ 20	122(24.21%)	243(27.74%)		
>20	140(27.78%)	225(25.68%)	21.8899	<.0001
Insemination method				
IVF	419(83.13%)	736(84.02%)		
ICSI	59(11.71%)	103(11.76%)		
IVF+ICSI	26(5.16%)	37(4.22%)	0.6432	0.725
Embryos transferable	3.41±2.69	4.81±2.91	8.84	<.0001
Numbers of embryo transferred	1.78±0.43	1.79±0.4	0.49	0.6252

Table3 Crude and aHR for cumulative live birth rate (CLBR) of women with PCOS

Independent covariates	Covariate strata	Crude hazard ratio (95% CI)	P-value	aHR (95% CI)	P-value
AGE(Years)	<30	-			
	30-34	0.89(0.75-1.05)	0.175	0.92(0.77-1.1)	0.3541
	35-38	0.79(0.51-1.21)	0.2775	0.93(0.59-1.47)	0.7607
	>38	0.52(0.17-1.61)	0.2537	0.72(0.23-2.25)	0.5674
Duration of Infertility (Years)	0 ~ 2	-			
	3 ~ 4	0.94(0.79-1.12)	0.48	0.88(0.73-1.05)	0.1029
	>4	0.8(0.67-0.96)	0.015	0.78(0.64-0.94)	0.0895
Type of Infertility	Primary Infertility	-			
	Secondary Infertility	0.86(0.75-1)	0.0459	0.85(0.72-0.99)	0.5403
Treatment Protocols	Prolonged GnRH-agonist	-			
	GnRH-agonist	0.7(0.57-0.85)	0.0004	0.63(0.5-0.8)	0.1598
	GnRH-antagonist	0.67(0.46-0.97)	0.0356	0.71(0.48-1.06)	0.0094
	Mild Stimulation	0.35(0.14-0.83)	0.0175	0.4(0.15-1.08)	0.0001
Start Dose of Gonadotrophins (IU)	<100	-			
	100	1.2(0.94-1.54)	0.1362	1.24(0.96-1.59)	0.0968
	112.5	1.27(1-1.62)	0.0497	1.24(0.97-1.6)	0.0698
	>112.5	0.78(0.56-1.08)	0.1278	0.9(0.64-1.27)	0.0358
Oocytes Retrieved	1 ~ 10	-			
	11 ~ 15	1.54(1.26-1.88)	<.0001	1.54(1.25-1.89)	<.0001
	16 ~ 20	1.29(1.05-1.58)	0.0151	1.28(1.04-1.58)	0.0221
	>20	0.95(0.77-1.17)	0.6203	0.95(0.76-1.18)	0.6249

Figures

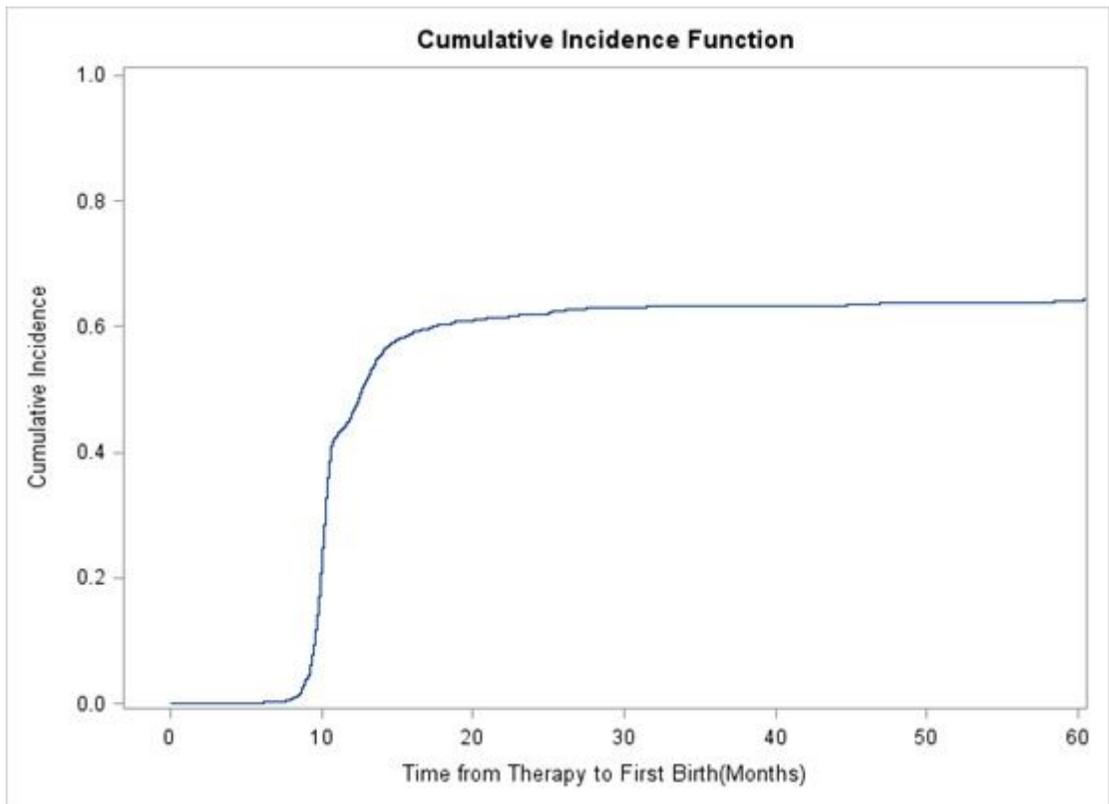


Figure 1

Cumulative live birth rates (CLBRs) in PCOS patients including all first deliveries during 2-4 years follow-up

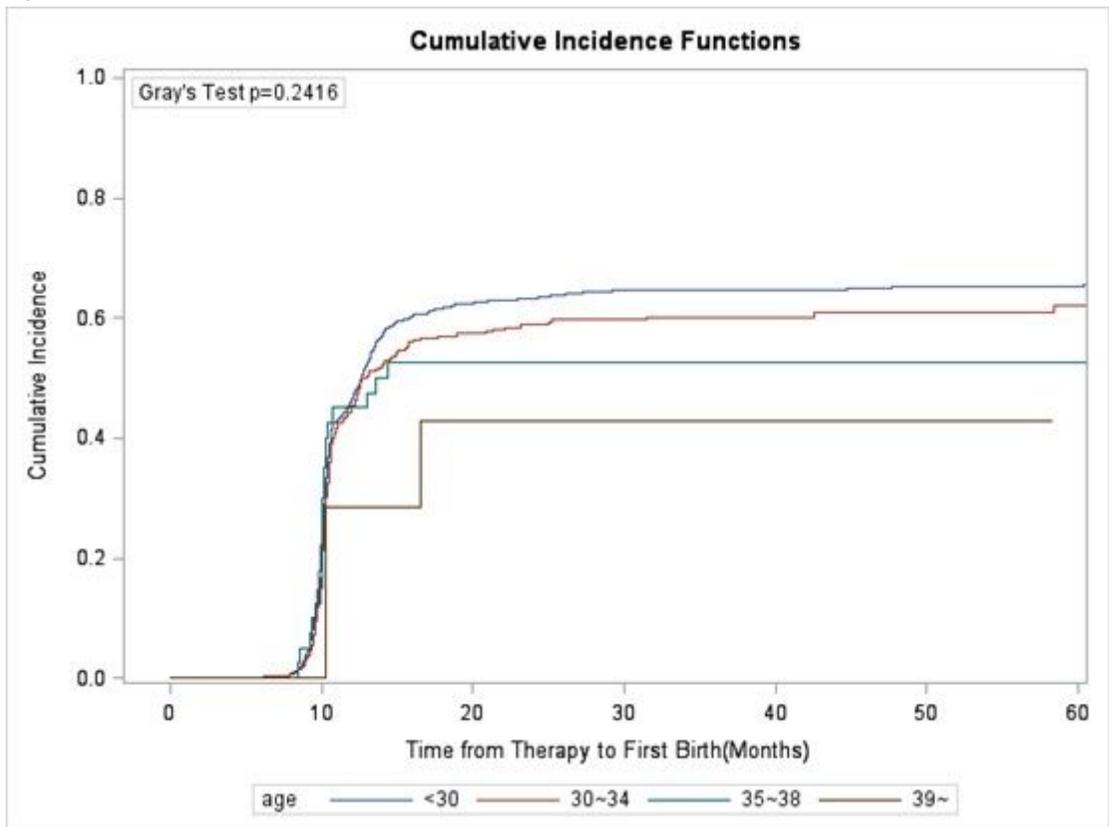


Figure 2

CLBR, stratified for age in three groups <30 years, 30–34 years, 35-38 years and >36 years. The distributions were similar ($P = 0.2416$),

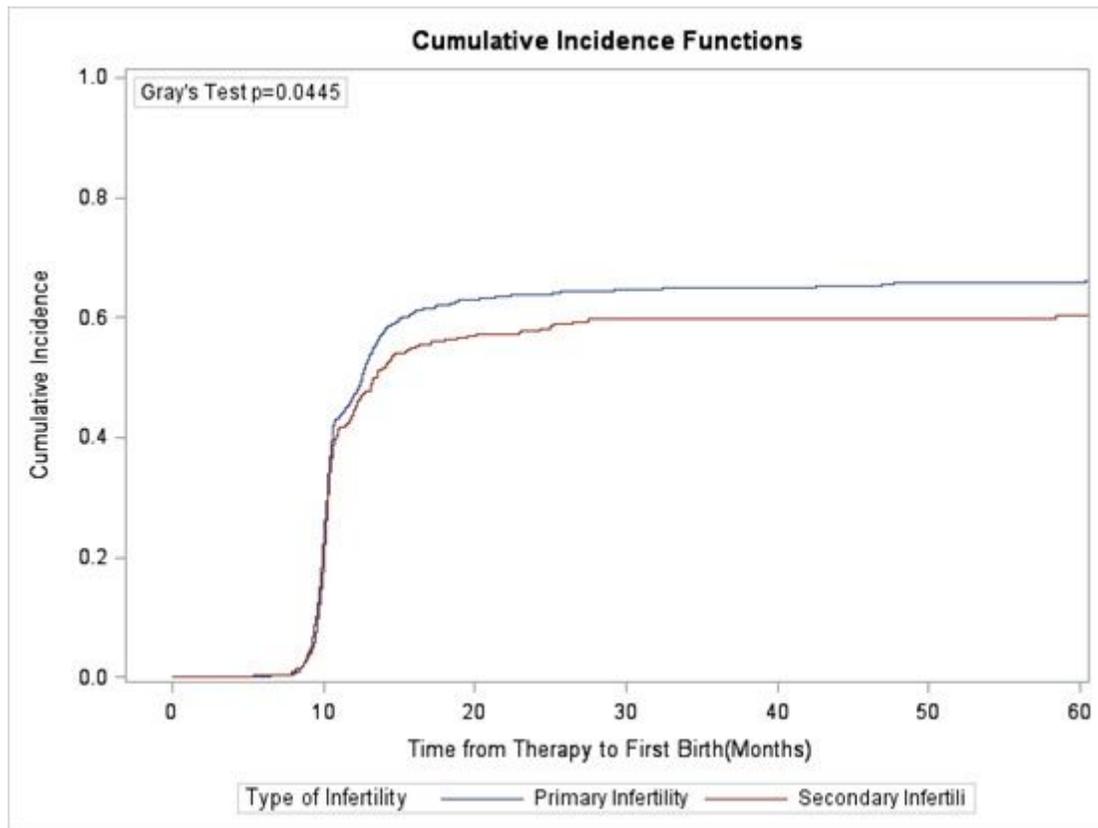


Figure 3

CLBRs in PCOS patients with secondary infertility were significantly higher than the people with Primary infertility ($P=0.0445$).

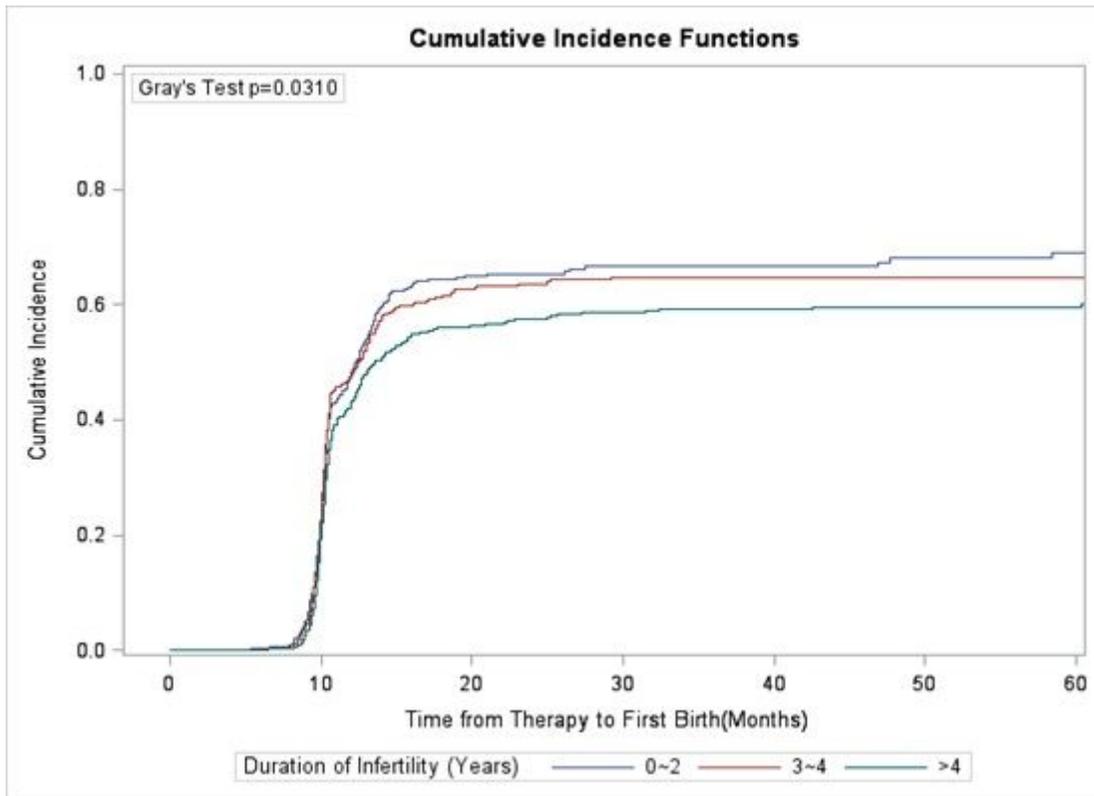


Figure 4

CLBRs, stratified for duration of infertility years in three groups 0-2, 3-4 and 4- . The distribution differed significantly ($P =0.031$).

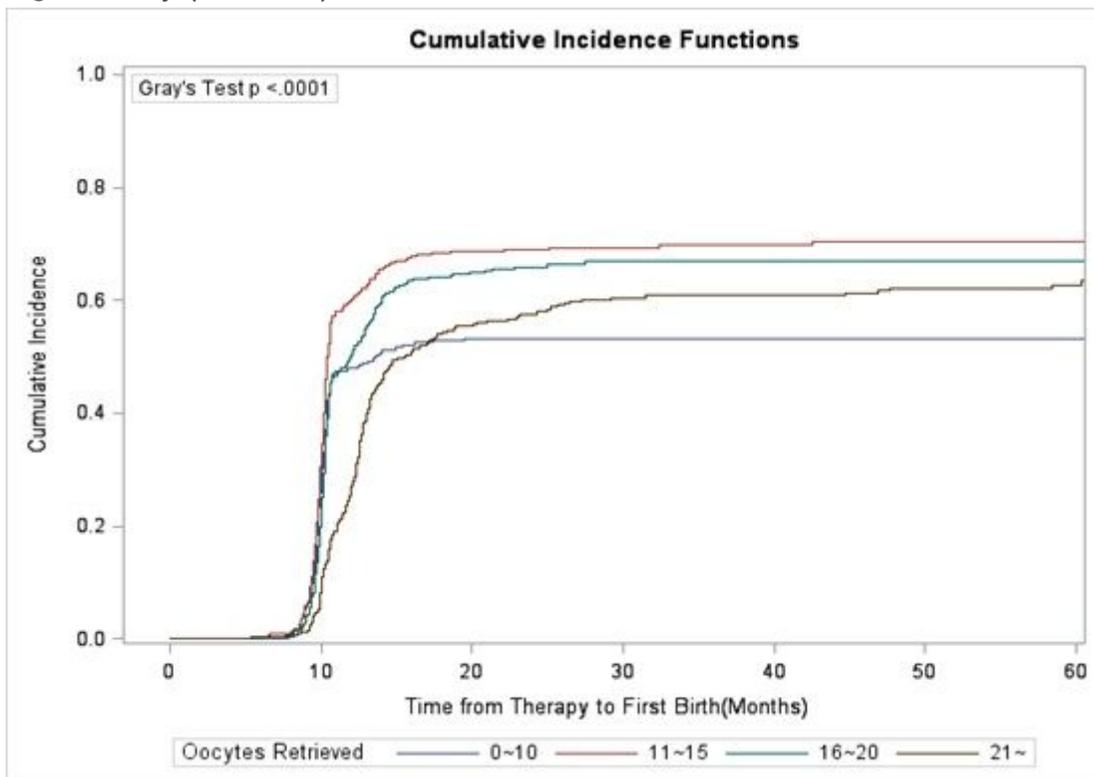


Figure 5

CLBRs, stratified for number of retrieved oocytes in four groups 0–10, 11–15, 16–20 and >20 oocytes. The distribution differed significantly in the groups ($P < 0.0001$).

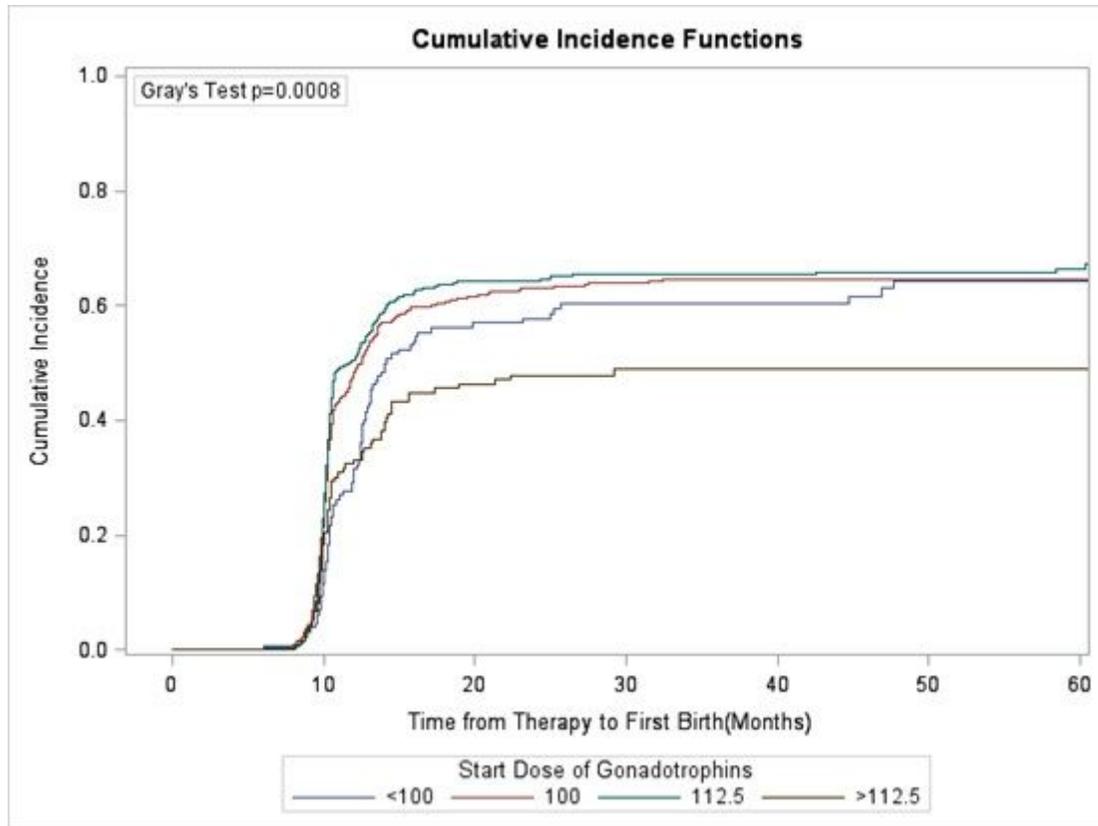


Figure 6

CLBRs, stratified for start dose of gonadotrophins in four groups <100IU, 100IU, 112.5IU and >112.5IU. The distribution differed significantly in the groups ($P < 0.0008$).

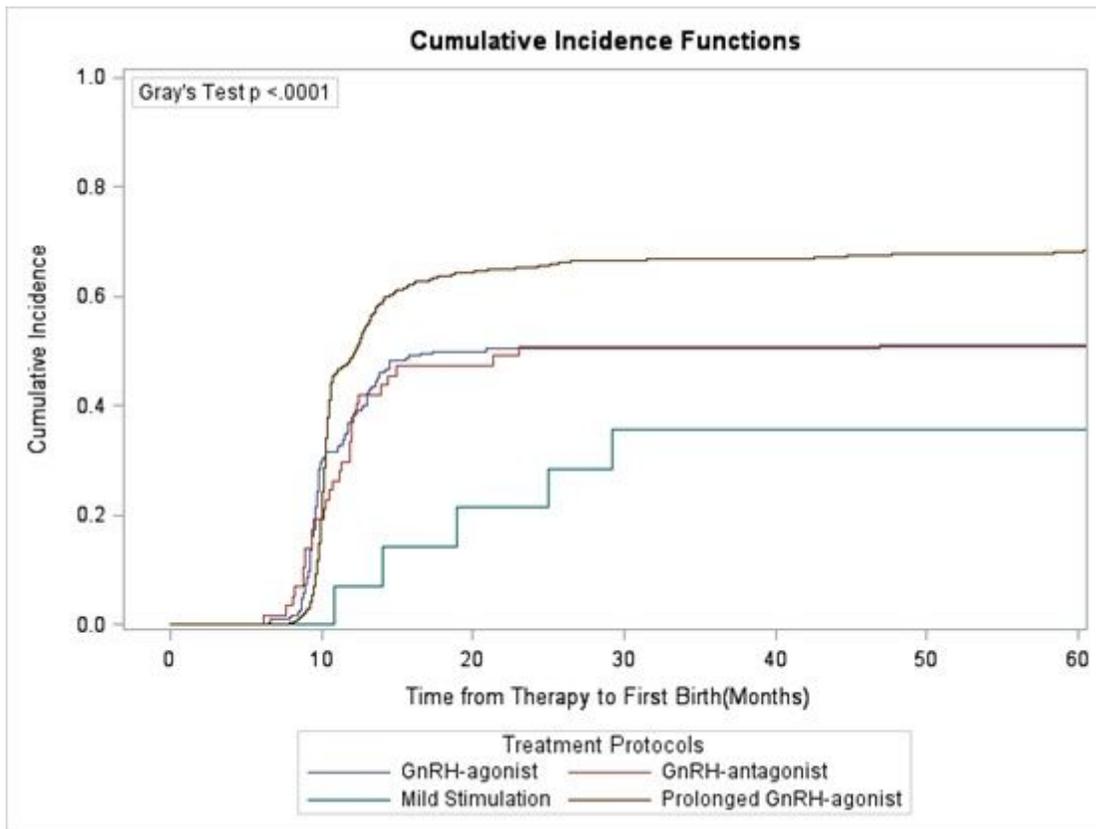


Figure 7

CLBRs, stratified for treatment protocols in four groups Prolonged GnRH-agonist, GnRH-agonist, GnRH-antagonist and Mild Stimulation. The distribution differed significantly in the groups ($P < 0.0001$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Patientinformationincludedinstatistics.xlsx](#)