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Received: 29 Dec 2022 - Accepted: 25 Feb 2024 - Published: 16 Apr 2024

Keywords: Oocyte recovery rates (ORR), in-vitro fertilization, Nigerian women

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Cite this article: Amina Mohammed-Durosinlorun et al. Factors associated with oocyte recovery rates during in-vitro fertilization among Nigerian women. Pan African Medical Journal. 2024;47(190). 10.11604/pamj.2024.47.190.38674

Available online at: https://www.panafrican-med-journal.com//content/article/47/190/full

Factors associated with oocyte recovery rates during in-vitro fertilization among Nigerian women

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Abstract

Introduction: the availability of oocytes is fundamental to in vitro fertilization (IVF). The factors associated with optimal or suboptimal oocyte recovery rates (ORR) in low-resource settings are not well known. This study aimed to determine the factors associated with ORR by comparing demographic and IVF cycle data of women undergoing IVF in our Centre. Methods: this was a prospective study of 110 infertile women undergoing IVF at Nisa Premier Hospital, Abuja Nigeria, from October 2020 to September 2021. All women had reached the stage of oocyte retrieval or further, after receiving ovarian stimulation with our routine protocols. Treatment was monitored by serial transvaginal ultrasonography. The oocyte retrieval procedures were performed under conscious sedation, 36 hours after the ovulatory trigger. Optimal ORR was when eggs were obtained from at least 80% of follicles punctured. Suboptimal ORR was when it was less than 80%. Data analyses utilized SPSS statistical software and a pvalue of < 0.05 was considered significant. **Results:** the mean age of all women was 34.1±4.9 years. Sixty-nine women (62.7%) had sub-optimal ORR while 41 (37.3%) had optimal ORR. Six women (5.5%) had no oocytes retrieved. Significantly more women with sub-optimal ORR were obese (70.6 vs 29.4%) and had higher follicle-stimulating hormone FSH levels (8.11 vs 6.34 miu/ml), p-value- 0.039. Women with sub-optimal ORR had higher mean prolactin levels (17.10 ± 13.93 miu/ml) than women with optimal ORR 11.43 ± 6.65 miu/ml), p-value-0.019). Significantly more oocytes (5.99 vs 10.37, pvalue 0.001), and MII oocytes (5.78 vs 7.56, p-value 0.035) were retrieved in women with optimal than sub-optimal ORR. The duration of stimulation, total amounts of gonadotropins administered, and fertilized oocytes were not significantly different among both groups (p-value >0.05). Conclusion: this study has shown the factors associated with ORR in our setting to be basal FSH, prolactin, and obesity.

Introduction

Infertility occurs if there is a failure to achieve pregnancy after one year of regular, unprotected sexual intercourse [1,2]. It is of significant public health concern [3,4] with an estimated worldwide prevalence of 8-12% [2]. Prevalence is much higher in sub-Saharan Africa [5-8] Nigeria is included in the demographic infertility African belt, paradoxically has both high fertility rates, coexisting with high infertility rates [3]. Some studies (mostly facility-based) have quoted the prevalence of infertility within Nigeria, as 26.8% in Lagos [9], 15.4% in Abakaliki [10], 15.7% in Sokoto [11], and 23.9% in Bauchi [12]. The prevalence may be on the rise as more women delay childbearing for education, work, and other reasons [3,13].

The adverse effects of infertility especially by women, are exaggerated in our environment due to cultural expectations and fertility preferences [14]. These negative effects include social isolation, neglect, abuse, physical violence, marital discord, stigmatization, and depression [15]. Overall, the quality of life is reduced. In trying to overcome their infertility, couples may face long, frustrating, and expensive treatments without full guarantees of success [16]. The aetiology of infertility also varies widely with contributions from both the male (30-40%), and the female partner (30-40%), and combined/sometimes it is unexplained (20-40%) [17]. Among the various causes of infertility, tubal factor infertility is more common in this environment, related to complications of sexually postabortal, transmitted, and postpartum infections [18-24]. This form of infertility is best treated with assisted reproductive techniques (ART) [21,24]. Assisted reproductive techniques may also be the last option for couples with infertility if other treatments have failed. In-vitro fertilization (IVF) is one of the most widely used interventions for infertility [25]. One Nigerian study estimated that 24.5% of the studied population would require and benefit from ART [26].



Assisted reproductive techniques involve in vitro manipulation of the gametes. Pioneering work in Cambridge by Steptoe and Edwards lead to the birth of Louise Brown, the first IVF baby. The field of ART has since grown, and a lot of new drugs and techniques introduced to improve success. By the end of 2013, five million IVF babies were born worldwide [27]. In Nigeria, over 40,000 babies have been born through IVF [28]. In Nigeria, the early work done by the likes of Ashiru and Giwa-Osagie in Lagos, Wada in Abuja, Orhue in Benin, and Ikechebelu in Nnewi has made ART widely available in some parts of Nigeria but is still inadequate to meet demands [28-30]

Oocyte retrieval is a critical step in the ART/IVF process as it's the only way to make the oocytes available for external fertilization. Furthermore, success at this stage is important to boost the morale of the couples. In the early days when IVF was performed using natural cycles, the target was the retrieval of one oocyte, thus the success rate at the time was low with a live birth rate (LBR) of 9.6% [31]. Subsequently, ovarian stimulation with drugs like clomiphene and gonadotropins led to multiple oocytes being retrieved and higher success rates [32,33]. In addition, excess eggs and embryos generated can be frozen and used later or even donated to research or use by other couples.

The reported oocyte recovery rate in natural cycles is 80% [34]. but with ovarian stimulation, the number of oocytes retrieved can be much lower than the number of follicles observed on ultrasonography. This can be because some follicles may develop but do not contain any oocytes [35]. The fact that at the end of an IVF stimulated cycle, few or no oocytes may be retrieved can be a disaster, more so if serial ultrasound scans had shown the presence of several promising follicles. The couple (and health care personnel) would have undergone a lot of psychological stress, sacrificed a lot of time, and spent a lot of resources without obtaining their objective [36,37].

A rare and controversial "empty follicle syndrome" (EFS) was first described by Coulam et al. in

1986 [38]. The reason for unsuccessful or suboptimal oocyte retrieval was not clear. It has however been attributed to iatrogenic and technical/drug-related causes (false EFS) [39,40], dysfunctional folliculogenesis with early oocyte atresia, genetic cause, ovarian aging, and poor ovarian response (genuine EFS) [40-44]. A borderline form of EFS has also been described as cases where very few mature or immature oocytes are retrieved from the aspiration of several follicles after a satisfactory ovarian stimulation regimen [45,46].

Despite developments of ART, 35-40% of couples remain childless after treatment hence science still has a lot to understand and develop to continuously improve success rates [47]. This study aims to investigate the factors affecting the disparity between follicles seen, and oocytes retrieved in stimulated IVF cycles among infertile Nigerian women. Fertility research is generally sparse in this environment despite the huge burden of infertility, cultural aversion to adoption or thirdparty treatments, and the high cost of ART, which makes the technology inaccessible to most people who need it in Nigeria [48,49]. So, sub-optimal oocyte retrieval constitutes an additional burden because it can potentially halt treatment. Very few studies have examined the disparity between follicles seen and oocytes retrieved during IVF. studies done previously have been retrospective or studied other related aspects like follicular size or volume [50-52]. There is a dearth of information from low-resource settings on ORR and it is expected that findings in this study would contribute to the body of knowledge on this subject. This may ultimately help counsel infertile couples planning to start IVF, stimulate further and direct the development of research, treatments to maximize oocyte retrieval, leading ultimately to improved success rates.

Methods

Design: this was a prospective study.



Setting: the study was carried out at the Nisa Premier Hospital (Nisa) located in Jabi, Abuja; Federal Capital Territory (FCT) Nigeria. The hospital has a capacity for 60 adult in-patient beds and 40 baby cots and provides a wide range of services in different specialties: general outpatient services, family medicine, obstetrics and gynaecology, surgery, and paediatrics among others [53]. The hospital does an average of 400-500 fresh/frozen IVF/ICSI cycles per year.

Study population: infertile women seen at the Nisa Premier Hospital from 1st October 2020 to 30th September 2021), Abuja with the following eligibility criteria.

Inclusion criteria: all infertile women ≥ 18 years coming for IVF/ICSI cycles that have been selected for controlled ovarian hyperstimulation during the study period (irrespective of if they have had previous stimulation or not), women with both ovaries present and visible on transvaginal ultrasound during follicular tracking, women whose oocyte retrieval (OCR) was done via the transvaginal route.

Exclusion criteria: women not willing to participate in the study, or whose cycles were canceled before oocyte retrieval, women with previous ovarian surgery, chemotherapy, or pelvic radiotherapy. Menopausal women undergoing third-party programs were excluded. Cycles with significant technical difficulties or complications during OCR leading to incomplete retrievals were excluded.

Sampling: a convenient sample of all patients meeting the study criteria over one year as stated earlier was used.

Procedure: all women who gave consent to participate in the study were recruited consecutively until the sample size was attained. After a proper history was taken and a physical examination done, routine infertility investigations were done. Routine hormonal measurements were done on day 3 (2-5) of the menstrual cycle. Ovarian stimulation was done using standardized agonist or

antagonist protocols. Protocols used and starting doses of drugs vary depending on factors such as age, hormonal levels, previous response, and risk of ovarian hyperstimulation. The dose was adjusted appropriately based on patients' responses. Usually, Buserellin was used for agonist cycles, cetrorelix (Cetrotide®, Merck Serono, Darmstadt, Germany) for antagonist protocols, and various gonadotrophins (Menopur- Ferring Pharmaceuticals, Copenhagen, Denmark; or Gonal-F, Merck Serono, Darmstadt, Germany).

Follicular tracking was done by experienced fertility doctors using multiple transvaginal ultrasonographic scans. Ultrasound were done using Voluson P8 scanning machines (GE Healthcare Technology). Serum oestradiol was also used to monitor the cycle. Human chorionic gonadotropin (hCG) or Buserelin trigger was given depending on the protocol when a leading follicle measured ≥18 mm in diameter. Oocyte retrieval was carried out 35-36 hours after trigger by ultrasound-guided transvaginal puncture using a single lumen needle (Kitazato) under sedation. Routine embryo transfer was done on days 2-5 as indicated. Sometimes cryopreservation required. Routine oocyte/embryo culture was done by a trained embryologist and 1 to 3 embryos were transferred on days 3-5 as indicated. Luteal support was usually initiated 1 day after oocyte pick-up. Clients were followed up for a minimum period of 2 weeks after embryo transfer and records were retrieved. Serum pregnancy test was done 10-12 days after embryo transfer (ultrasound 5-6 weeks later when possible).

Data collection: a data extraction form was used to record important demographic information and clinical correlates for each patient including demographic information, history about infertility and diagnosis, cycle/treatment characteristics protocol. including induction hormonal/laboratory and TVUS (transvaginal ultrasonography) data, OCR data, and oocyte characteristics. Patient records were checked later to determine pregnancy outcomes complications.

Article &



Data analysis: the primary outcome measure for our study was oocyte recovery rate (ORR) in stimulated IVF cycles among pregnant women. ORR defined as the number of retrieved/number of follicles (seen on ultrasound at the end of ovarian stimulation and before oocyte retrieval) x 100. The ORR was considered to be optimal if it was ≥80%, and sub-optimal if it was <80%. Other secondary outcomes included: empty follicle syndrome (EFS) defined as the complete failure to recover any oocytes during OCR, with and without a detectable serum β-hCG on the day of retrieval, Oocyte quality which was classified as good (MII with good polar body) or poor (MI, GVgerminal vesicle, EZ- empty zona or atretic). Fertilized eggs were confirmed by the presence of 2 pronuclei), and a confirmed pregnancy. A chemical pregnancy was defined as a serum hCG >10IU/I done 10-12 days after embryo transfer while a clinical pregnancy was defined as finding a gestational sac, foetal pole, and foetal heartbeat on ultrasound at 5-6 weeks of gestation.

Statistical analysis was done using IBM SPPS Statistics 22 (Armonk, NY: IBM Corp). Baseline characteristics were summarized using simple frequency tables. To investigate the factors that may affect ORR in stimulated IV cycles among infertile women, dependent variables (demographic and reproductive characteristics such as age, ethnicity, parity, previous miscarriage, BMI, menstrual cycle characteristics, infertility, and lifestyle characteristics) were compared with the independent variable (optimal and sub-optimal ORR) using Chi-square test/Fisher's exact test for categorical variables and t-test to compare group means of quantitative data. A p-value of < 0.05 was considered to be of statistical significance.

Ethical approval: ethical approval was obtained from the Nisa Premier Hospital ethical committee and informed consent from patients. Most of the information, procedures, and investigations were already part of the routine work-up that the patients undergo for IVF. So, there was no additional monetary or psychological cost to patients. If patients declined consent, the quality of

care they received was not affected. All patient identifiers were removed to maintain confidentiality.

Results

A total of 110 women were studied. Their baseline characteristics are shown in Table 1. Their mean age was 34.1±4.9 years, the median age of 35 years and, a range of 22 to 45 years. Most study participants were Hausa (49, 45.5%), multiparous (59, 53.6%), had no previous miscarriages (72, 65.5%), overweight or obese (74, 67.3%), had normal menstrual characteristics, had secondary infertility (59, 53.6%), with infertility for 1-5 years (72, 65.4%), with female factor infertility (69,62.7%), and received no previous fertility treatment (78. 70.9%). This is shown in Table 1. Sixty-nine women (62.7%) had sub-optimal ORR (<80%) while 41 women (37.3%) had optimal ORR (≥80%). Six women (5.5%) had no oocytes retrieved. The client's BMI (body mass index), the pattern of menstruation (regularity, length, and flow), and trigger type were significantly associated with ORR (P-value < 0.05) as shown in Table 2. When comparing means (Table 3), there were significant differences in FSH levels, prolactin levels, total number of oocytes retrieved, and number of MII (mature) oocytes. Though number of oocytes that got fertilized was slightly higher in the optimal ORR group compared to the sub-optimal group, the difference was not statistically significant.

Due to loss at follow-up, there was inadequate data on clinical outcomes to compare among the groups. There were 63 fresh cycles while the others had their cycle either canceled or converted to a frozen cycle (and some are yet to return) due to several reasons; no oocytes retrieved, only immature oocytes retrieved, progesterone was high, arrested growth especially after biopsy, high risk for ovarian hyperstimulation syndrome and spouse unable to make sperm available. Available data however showed 30 biochemical pregnancies/positive pregnancy tests (33 negative pregnancy tests, 47 missing data on pregnancy tests), 19 clinical pregnancies (11 singletons, 7 twins, and I triplet), 6



miscarriages, 1 live birth, and no cases of moderate or severe OHSS.

Discussion

During IVF, several studies agree that for each additional egg retrieved, the chances of having a live birth are increased, to the optimum of 6-15 eggs retrieved [54-56]. This study aimed to determine factors associated will non-retrieval of oocytes from follicles seen on ultrasound during ovarian stimulation leading to optimal or suboptimal ORR. Very few researchers have studied this, especially in our environment.

In our study, women who were overweight and obese had more sub-optimal, than optimal ORR (p-value <0.05) (Table 2). Extremes of weight have traditionally been associated with poor fertility outcomes though studies give controversial results. One cohort study of 342 treatment cycles reported sub-optimal outcomes including significantly fewer mature (MII) oocytes in overweight women, but this was only in the first treatment and suggested an effect modification related to the treatment cycle number [57]. Other studies however showed that being overweight or obese did not adversely affect ovarian function [58]. It may seem wise to continue to advise women to be of optimal weight before embarking on IVF treatment.

The menstrual pattern was significantly associated with ORR (Table 2). This is probably because a regular menstrual cycle is assumed to be a reflection of normal levels of reproductive and regulatory hormones that would result in ovulation [59]. Women with polycystic ovarian syndrome (PCOS) are also known to have irregular menstrual cycles. In a study of 1834 women with PCOS undergoing IVF, women with amenorrhoea had significantly higher incidence of adverse pregnancy outcomes like abortion, preterm births, gestational diabetes, hypertension, premature rupture of membranes and macrosomia [60]. A study of fertility and menstrual patterns in 470 showed that conception following women menstrual cycles of abnormal length were more

likely to be aborted, while cycle flow of more than 5 days was associated with fewer abortions [59]. A cycle flow of 5 days also had the highest fecundity [59]. Perhaps the association of menstrual patterns and ORR may be due to the underlying cause of abnormal menstruation patterns such as PCOS, underlying hormonal dysfunction, or some unexplained cause requiring further study.

In our study, the mean FSH levels were significantly associated with ORR, higher in the sub-optimal group (Table 3). This is similar to findings from a Pakistani study, where a higher basal FSH follicle was significantly correlated with a higher incidence of EFS [61]. Women with diminished ovarian reserve have higher FSH to try and compensate, and generally have poorer response to ovarian stimulation and IVF outcomes, especially if FSH levels are above 18 IU/L [62]. The trio of BMI, FSH and abnormal menstrual patterns found in this study to be related to ORR may not be unrelated to a PCOS [63].

Prolactin levels were also associated with ORR in our study. Hyperprolactinaemia (serum prolactin > 25 ng/ml) is a known cause of anovulation and infertility. Prolactin may however have a role in oocyte maturation and embryonic development, as some studies found that higher basal prolactin levels (> 16.05 ng/mL) were associated with larger numbers of mature oocytes and good-quality embryos. This contradicts our finding as the mean levels of prolactin were higher in the sub-optimal ORR group. Both groups in our study however had prolactin levels $\leq 50 \text{ ng/mL}$, and some studies have suggested that prolactin levels $\leq 50 \text{ ng/mL}$ may not require any treatment [64,65].

In this study trigger type was significantly associated with ORR, with more women using HCG having optimal ORR than Buserelin (Table 2). The natural LH surge is longer (48 hours) as compared to the GnRH analogue induced LH surge (28-32) but the implications of this are unclear, and some studies show that choice of trigger may not increase the incidence of EFS [66,67]. An additional



benefit of GnRH analogue for the trigger is that it also induces an FSH surge, keeping gap junctions open between the oocyte and cumulus cells, and plasminogen facilitating activates follicle detachment [68]. Human chorionic gonadotropin does not provide this additional FSH surge, and the use of dual triggers has been suggested [65]. chorionic gonadotrophin Human or GnRH (gonadotrophin-releasing hormone) analogues can be used as natural LH (luteinising hormone) substitutes [69] to trigger the final maturation of oocytes [70,71]. They also induce the meiotic reactivation of the oocyte and enhance the detachment of the cumulus-oocyte complex from the follicle wall [70].

The optimal ORR group had a significantly higher mean number of MII (mature) oocytes which is not surprising. They also had a higher mean number of fertilized eggs, but this was not statistically significant. This is similar to findings from another study, where a low follicle-oocyte index while not significantly affecting outcomes, merely presented an opportunity for research to exploit new therapies to maximise oocyte yield and overlap prognosis [72]. Empty follicle syndrome, an extreme form of sub-optimal ORR where no oocytes at all are retrieved can be quite devastating and occurred in only six women. They are more likely due to the genuine form as all precautions are taken to prevent technical or drug-related causes. A lot of women in this environment advised on third-party treatments (due to advanced age or other features that may suggest poor ovarian response) still prefer to try with their eggs and some still succeed. Repeating triggers, dual triggers with another batch of HCG and repeating oocyte retrieval may be useful in such cases [73,74].

Study limitations: this study contributes to the dearth of fertility studies in this environment. However, it does have some limitations. This was a small study, and a timed convenient sample was used so results should be interpreted with some caution. Findings cannot be over-generalized as the sample is not representative of the whole population of Nigerian infertile women. Inter and

intra-observer errors may have introduced some bias and subjectivity during follicular tracking (ultrasonography), partly reduced by defining optimal ORR as a range. Stimulation protocols and drugs used were not uniform, and not all possible confounders were controlled for. Better data keeping and follow-up would have helped track other clinical long-term outcomes, though this was not the focus of this study.

Conclusion

ORR was significantly associated with BMI, pattern of menstruation (regularity, length and flow), trigger type, FSH levels, prolactin levels and number of MII oocytes. Having sub-optimal ORR however does not necessarily translate to significantly lower fertilization rates. More studies are however required, especially for relevance to other clinical outcomes. Studies to determine genetic causes of genuine EFS in this environment will also be useful. Communication with patients should continue after treatment irrespective of outcome.

What is known about this topic

- During ART some women are known to have poor responses;
- Follicles retrieved may differ from baseline antral follicular count but should correlate number seen at the trigger;
- Yet some women may even have empty follicle syndrome, which in genuine cases is difficult to treat.

What this study adds

- Baseline data which is scarce in African settings;
- Additional potential marker, ORR, that can be used to monitor ART quality and outcomes;
- Reveals possible factors in this environment that may be associated with the number of follicles retrieved that may be explored further and modified to improve outcomes.



Competing interests

The authors declare no competing interests.

Authors' contributions

Amina Mohammed-Durosinlorun contributed to the concept and design, the definition of intellectual content, literature review, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review. Ibrahim Wada contributed to the design, literature review, manuscript editing, and manuscript review. All the authors have read and agreed to the final manuscript.

Acknowledgments

We would like to thank the IMSA/NISA team for their help and encouragement.

Tables

Table 1: baseline characteristics of participants **Table 2**: association between demographic, reproductive, and other variables with ORR **Table 3**: comparison of variable means between optimal and sub-optimal ORR groups

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Table 1: baseline characterist	ics of participants	_	
Characteristics		Frequency	Percent
Age	<30	22	20
	30-34	30	27.3
	35-39	43	39.1
	≥ 40	15	13.6
Ethnicity	Hausa	49	45.5
	Igbo	27	24.5
	Yoruba	15	13.6
	Others	19	17.3
Parity	0	51	46.4
	1-4	54	49.1
	≥ 5	5	4.5
Previous miscarriage	No	72	65.5
-	Yes	38	34.5
Body mass index (BMI)	< 18.5 (underweight)	0	0
· ,	18.5 - <25 (normal weight)	6	5.5
	25 - <30 (overweight)	40	36.4
	≥ 30 (obese)	34	30.9
	Missing	30	27.2
Menstrual characteristics	Age at menarche (years)		
	10 🛽 16	87	79.1
	≥ 17	5	4.5
	Missing	18	16.4
Cycle regularity	Regular	89	80.9
-, ere regerment,	Irregular	15	13.6
	Missing	6	5.5
Cycle length (days)	212 35	101	91.8
eyere rengan (aaye)	>35	2	1.8
	Missing		6.4
Flow duration (days)	2-8	99	90
(42,75,	≥ 9	5	4.5
	Missing	6	5.5
Type of infertility	Primary	51	46.4
	Secondary	59	53.6
Duration of infertility (years)		10	9.1
	1-5	72	65.4
	6-10	18	16.4
	>10	10	9.1
Cause of infertility	Male factor	10	9.1
	Female factor	69	62.7
	Combined	23	20.9
	Unexplained	8	7.3
Lifestyle>	Drinks		
	No	104	94.5
	Yes	6	5.5
Smokes	No	108	98.2
		2	1.8
Sillokes			T.O
	Yes No		
	No Yes	78 32	70.9 29.1





Table 2: association between	demographic, reproducti	1			
	A	ORR	1	Test statistic and p- value	
Variables	Age		≥ 80%		
	<30	15(68.2)			
	30-34			X2- 9.868, df-6, p-value-0.140	
	35-39	25(58.1)	• •		
	≥ 40	13(86.7)	2(13.3)		
•	Hausa	31(63.3)	18(36.7)	X2- 1.113, df-3, p-value-0.774	
	Igbo	18(66.7)	9(33.3)		
	Yoruba	10(66.7)	3(33.3)		
	Others	10(52.6)	9(47.4)		
Parity	0	32(62.7)	19(37.3)	Likelihood ratio- 0.761, df-2, p-value-0.684	
	1-4	33(61.1)	21(38.9)		
	≥ 5	4(80)	1(20.0)		
Previous miscarriage				X2- 0.580, df-1, p-value-0.446	
	Yes	22(57.9)		, , ,	
		6(100.0)		Likelihood ratio- 8.359, df-3, p-value-0.039	
2004 mass mass (2mm,		21(52.5)			
	` '	24(70.6)			
	Missing	18(60.0)			
	Age at menarche (years)	±0(00.0)	±∠(4 ∪)	Likelihood ratio- 5.472, df-2, p-value-0.065	
vienstruation		E0/66 7\	20/22 21	Likeiiii00d ratio- 3.472, di-2, β-vaide-0.003	
		58(66.7)			
	≥ 17	<u> </u>	1(20.0)		
	Missing	7(38.9)		h., ., ., ., ., ., ., ., ., ., ., ., ., .	
Cycle regularity	Regular			Likelihood ratio-12.830, df-2, p-value-0.002	
	Irregular	11(73.3)			
	· ·		6(100)		
				Likelihood ratio- 9.199, df-2, p-value-0.010	
		2(100.0)	` '		
		1(14.3)			
	2-8	68(68.7)	31(31.3)	Likelihood ratio-17.209, df-2, p-value-0.000	
	≥ 9	1(20.0)	4(80.0)		
	Missing	0(0)	6(100)		
Type of infertility	Primary	32(62.7)	19(37.3)	Likelihood ratio- 0.000, df-1, p-value-0.997	
	Secondary	37(62.7)	22(37.3)		
Duration of infertility (years)	< 1	5(50.0)	5(50.0)	Likelihood ratio- 4.926, df-3, p-value-0.177	
	1-5	45(62.5)	27(37.5)	·	
	6-10	10(55.6)			
		9(90.0)			
Cause of infertility	Male factor			Likelihood ratio- 3.416, df-3, -value-0.332	
		43(62.3)		2.410, di 3, value 0.332	
	Combined	17(73.9)			
		3(37.5)			
Lifostylo	Drinks	3(37.3)	3(02.3)	Likelihood ratio- 2.251, df-, p-value-0.133	
Smokes		(7/(4.4)	27/25 ()	•	
		67(64.4)			
		2(33.3)		hii iii 1 1 2 2 2 2 2 2 2 2	
				Likelihood ratio- 4.010, df-1, p-value-0.045	
	Yes		2(100.0)		
	No			Likelihood ratio- 1.615, df-1, p-value-0.204	
		23(79.1)			
•				X2- 0.023, df-1, p-value-0.880	
	Antagonist	36(62.1)	22(37.9)		
Trigger type	Buserelin	11(44)	14(56)	Likelihood ratio- 12.124, df-2, p-value-0.00	
	HCG	57(72.2)	22(27.8)		
	Missing	1(16.7)			
Serum pregnancy test	Negative			X2- 8.756, df-2, p-value-0.013	
	Positive	13(43.3)			
		36(76.6)			
			\ \ /		





Variable	ORR groups			
	Sub-optimal ORR (<80%)	Optimal ORR (≥ 80%)		
Mean age (years)	34.55 ± 5.29 (69)	33.37 ± 4.15 (41)	0.195	
Total gonadotrophin use (I.U)	3291.41 ± 1390.38 (68)	3377.08 ± 1172.70 (36)	0.848	
Duration of stimulation (days)	10.66 ± 1.3 (68)	10.64 ± 0.96 (36)	0.926	
Peak oestradiol (E2) (pg/ml)	3218.63 ± 4897 (66)	3897.99 ± 6611 (36)	0.559	
AMH (ng/ml)	2.48 ± 2.51 (5)	3.96 ± 2.39 (11)	0.278	
FSH (miu/ml)	8.11 ± 4.46 (68)	6.34 ± 3.70 (39)	0.039	
LH (miu/ml)	3.67 ± 2.39 (68)	3.92 ± 2.57 (40)	0.614	
Prolactin (miu/ml)	17.10 ± 13.93 (68)	11.43 ± 6.65 (39)	0.019	
Progesterone (ng/ml)	4.04 ± 3.42 (35)	3.27 ± 2.90 (19)	0.411	
Basal AFC	11.31 ± 5.94 (68)	11.46 ± 6.30 (41)	0.898	
Total follicles (trigger day)	10.32 ± 6.46 (69)	10.83 ± 6.67 (41)	0.093	
Number retrieved oocytes	5.99 ± 4.89 (69)	10.37 ± 6.32(41)	0.001	
Oocytes >14-16mm	7.96 ± 4.95 (69)	8.20 ± 5.05 (41)	0.809	
MII oocytes	5.78 ± 3.86 (58)	7.56 ± 4.42 (41)	0.035	
Number fertilized	5.30 ± 3.82 (57)	6.71 ± 3.96 (41)	0.079	

Note: values are mean ± standard deviation (number of clients), AMH: anti mullerian hormone, FSH: follicle stimulating hormone, LH: luteinizing hormone, AFC: antral follicular count, ORR: oocyte recovery rate