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Original Articles

Responses and Reproductive Outcomes Across Four Ovarian Stimulation Protocols in Poor Responders: A Retrospective Cohort Study

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Abstract

Background: The optimal approach to ovarian stimulation in poor responders remains controversial. This study aimed to compare four stimulation treatment protocols to improve reproductive outcomes in patients undergoing controlled ovarian hyperstimulation prior to in-vitro fertilization/intracytoplasmic sperm injection under gonadotropin-releasing hormone antagonist regimens.

Methods: A retrospective cohort study was conducted among poor responder female patients. The participants were divided into four groups according to treatment protocol—Group 1: High-dose rFSH (≥300 IU) with rLH; Group 2: hMG with rFSH (≥300 IU); Group 3: rFSH (≥300 IU/day) alone; Group 4: hMG (≥300 IU) alone —and followed up to determine their reproductive outcomes.

Results: A total of 157 poor responders were included. Baseline characteristics were comparable across the four treatment groups, with no significant differences in age, BMI, duration of infertility, or basal E2, PRL, and TSH levels. Basal FSH and LH levels showed statistically significant differences between groups (p=0.049 and p=0.007, respectively), although median FSH values were similar overall. Causes of infertility did not differ significantly among groups.

Treatment duration, final E2 levels, follicle numbers, oocyte yield, embryo numbers, and ICSI outcomes were comparable across groups. However, total gonadotropin dose differed significantly, with the rFSH + LH group requiring the highest dose. Pregnancy outcomes—including positive pregnancy test rates, clinical pregnancy, implantation, and live birth rates—were not significantly different among treatment groups. Miscarriage history differed significantly, with the highest proportion observed in the hMG group (p=0.046). Of 135 patients undergoing embryo transfer, 39.3% (n=53) had positive pregnancy tests, resulting in 28 live births. No ectopic pregnancies occurred. Live birth distribution did not differ significantly by age group or treatment regimen (p=0.553).

Conclusions: rFSH doses higher than 300 IU did not significantly alter reproductive outcomes, raising the question of whether such high doses of gonadotropins are advisable in this patient population.

Keywords: Embryo Transfer, Fertilization in Vitro, Follicle Stimulating Hormone, Gonadotropin-Releasing Hormone, Gonadotropins, Intracytoplasmic, Menotropins, Ovarian Reserve, Ovulation Induction, Retrospective Studies, Sperm Injections.

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INTRODUCTION

Infertility has become a global issue, with the World Health Organization (WHO) recently reporting that approximately 17.5% of the adult population—roughly 1 in 6 worldwide—experience infertility at least once during their reproductive lifetime [1]. Various assisted reproductive technologies have been developed to treat infertility. One such is in-vitro fertilization (IVF) [2,3]; another is intracytoplasmic sperm injection (ICSI). IVF and ICSI typically conclude with an embryo transfer procedure, in which a previously selected embryo is placed in the uterus or the Fallopian tube [2]. However, poor ovarian response (POR) will be experienced in 5.6% to 35.1% of patients [4,5].

POR refers to the inability of the ovary to respond appropriately to standard stimulation and recruit sufficient follicles. This results in reduced oocyte production, cycle cancellation, and a generally markedly lower likelihood of pregnancy [6]. According to the Bologna Criteria, introduced by the European Society of Human Reproduction and Embryology (ESHRE), a poor ovarian responder (POR) meets at least two of the following three criteria: (i) aged 40 years or older, or any other risk factor; (ii) previous poor ovarian response (cycles canceled or ≤3 oocytes with a conventional protocol); (iii) abnormal ovarian reserve test (ORT) (antral follicle count (AFC) 5–7 follicles, or anti-Mullerian hormone (AMH) 0.5–1.1 ng/ml) [7]. In the absence of advanced maternal age or abnormal ORT, two previous episodes of POR after maximal stimulation are sufficient to consider a patient a poor responder [8]. This cohort is challenging to treat and represents a great proportion of patients presenting with infertility; their treatment has thus been the focus of numerous randomized trials over the past two decades [9].

The optimal approach to ovarian stimulation in poor responders is a debated topic. Various protocols have been proposed for optimizing IVF/ICSI outcomes in cases of inadequate response to controlled ovarian stimulation; nonetheless, achieving a good response remains a challenge in this population [10]. The most widely employed approach to improving follicular response in these so-called 'poor responders' utilizes high doses of gonadotropins. Also, luteinizing hormone (LH) supplementation during the early phase of the stimulation protocol may have a beneficial effect on the maturity and developmental competence of oocytes, as well as the number of embryos transferred. However, published data from one study do not conclusively demonstrate improved pregnancy rates in patients who received LH in addition to recombinant follicle-stimulating hormone (FSH) [11]. Additionally, one retrospective study found that poor responders do not benefit from high doses of human menopausal gonadotropin (hMG) [12].

Recent studies and various recommendations from the scientific community propose a more patient-friendly approach, indicating the potential for low-dose gonadotropin, mild stimulation, LuPOR, and DuoStim protocols as novel strategies to improve outcomes and offer alternatives for poor responder patients [13].

The inconsistency of the evidence compounds the challenges faced by healthcare providers in treating poor responders. This study aimed to compare the effectiveness of four different protocols for improving ovarian response and pregnancy rates in poor responders undergoing controlled ovarian hyperstimulation (COH) prior to IVF/ICSI in gonadotropin-releasing hormone (GnRH) antagonist regimens.

METHODS

Study Design and Setting

A retrospective cohort study was conducted, between January 2016 and January 2018, in the Department of Reproductive, Endocrine, and Infertility Medicine at the Women's Specialized Hospital of King Fahad Medical City (KFMC), in Riyadh, Saudi Arabia.

Study Participants

The study included all female Saudi IVF/ICSI patients aged between 18-47 years who were characterized as POR according to the ESHRE's Bologna Criteria [7]. Also included were patients of normal maternal age and normal ORT, provided they had experienced two episodes of POR after maximal stimulation and high-dose gonadotropin (≥ 300 IU). All those with severe liver disease, kidney disease, lung disease, anemia, or blood clotting disorder were excluded from the study.

The participants were divided into four groups according to their treatment protocol: Group 1 received high-dose recombinant follicle stimulating hormone (rFSH) (≥ 300 IU) with recombinant luteinizing hormone (rLH); Group 2 received human menopausal gonadotropin (hMG) with rFSH (≥300 IU); Group 3 received rFSH (≥ 300 IU/day) alone; and Group 4 received hMG (≥ 300 IU) alone. The participants were then followed up to determine their reproductive outcomes.

Treatment Protocol

Patients underwent COH according to the standard GnRH antagonist protocol. For COH, patients received rFSH alone (Gonal-F®; Serono Inc., Rockland, MA, USA); or rFSH with rLH (Luveris; EMD Serono, Rockland, MA, USA) at a ratio of 2:1; or hMG alone (Merional; IBSA Institute Biochimique SA, Switzerland); or rFSH combined with hMG. In the group receiving the rFSH/hMG combination, the total combined dose was 450 IU: either 300 IU rFSH + 150 IU hMG, or vice versa. The minimum starting dose of gonadotropins was 300 IU; if an increase was necessary due to low estradiol on day 5 or 6 of stimulation, the dose was increased to 450 IU.

The GnRH antagonist, cetrorelix acetate (Cetrotide; Serono Inc., Rockland, MA, USA), was administered via daily injections of 0.25 mg, commencing on day 5 or 6 of menses or when the leading follicle was 13-14 mm in diameter, and continued daily until at least 3 leading follicles reached a mean diameter of 17 mm, whereupon human chorionic gonadotrophin (hCG) injections were commenced (Pregnyl; Merck, Kenilworth, NJ, USA).

Prior to commencing the protocol, each patient was assessed between days 2 to 4 of their menstrual cycle to ensure the absence of ovarian cysts, endometrial thickness of 6 mm on transvaginal ultrasound, and plasma E2 levels < 250 pmol/L [14]. Thereafter, treatment began with rFSH, hMG, or a combination at varying doses, as described above. After 5—6 days of stimulation, ovarian response was evaluated using E2 levels and ultrasound, and dosage adjusted accordingly using a step-up or step-down protocol. When two or more follicles had reached a minimum mean diameter of 17 mm, follicular maturation was achieved with urinary hCG at a dose of 10,000 IU intramuscular (IM). Transvaginal ultrasound-guided oocyte retrieval was performed 36 hours after hCG injection [14]. In cases where estradiol did not increase on two dose adjustments, or no follicular response was noted on ultrasound, or there was a premature surge of LH, the cycle was canceled. Retrieved oocytes were inseminated with sperm using IVF if the semen analysis was normal. Patients with severe male factor infertility or a history of fertilization failure in IVF underwent ICSI. Up to two fresh embryos were transferred on days 2–5 after fertilization. Patients were prescribed a 400 mg vaginal progesterone pessary (Cyclogest; Actavis, Barnstaple, UK) twice daily for luteal support, which continued for 10—12 weeks in the event of pregnancy. Clinical pregnancy was confirmed upon visualization on vaginal ultrasound of the gestational sac or heartbeat, along with an increasing beta-hCG level [15].

Data Collection

Data were collected using a standardized data collection form consisting of four sections. The first section covered demographic and clinical features, including age, body mass index (BMI) (kg/m2), years of infertility, and baseline levels of

FSH (mIU/mL), LH (mIU/mL), estradiol (E2) (pmol/L), prolactin (PRL) (ng/mL), and thyroid stimulating hormone (TSH) (μIU/mL). The second section detailed the participants' causes of infertility, which included anovulation, polycystic ovary syndrome, tubal factors, endometriosis, male factors, multiple causes, male/female factors, and unexplained causes. The third section included the clinical results of the different treatment groups; i.e., the duration and dose of FSH and rLH, final E2 and rLH levels on hCG day, number of oocytes collected, number of frozen embryos, number of inseminated ICSIs, number of fertilized ICSIs, number of embryos transferred (ET), and the day of ET. The fourth section detailed the participants' reproductive outcomes and pregnancy status, including positive pregnancy (defined as positive HCG 14 days after ET), biochemical pregnancy (defined as hCG ≥ 10 mIU/ml 14 days after ET), clinical pregnancy (confirmed by visualisation on vaginal ultrasound of the gestational sac or heartbeat, along with increasing beta-hCG level), as well as the implantation rate (defined as the ratio of gestational sacs with a fetal heartbeat to the total number of embryos transferred). As age also has a significant impact on ovarian reserve and the success of IVF, we also assessed the percentage of live births according to various participant age groups.

Ethical Considerations

The study was approved by King Fahad Medical City's R2 Institutional Review Board (IRB number 19-484E).

Sample Size Estimate

The total required sample size was estimated using G*Power software version 3.1.9.7. Based on *a priori* inputs, assuming 80% power, a significance level of $\alpha = 0.05$ (95% confidence interval), and a medium effect size of 0.27 across four groups, a total sample size of 156 was required to test for statistically significant differences between the means of the outcome (μ_i) measured across more than two groups with equal variance. These groups correspond to the 4 populations described above; i.e., High-dose rFSH (≥300 IU) with LH, rFSH (≥300 IU) alone, hMG (≥300 IU) alone, and hMG with rFSH (≥ 300 IU).

Statistical Analysis

Data were stored and managed using Microsoft Excel and the Statistical Package for Social Sciences (version 25.0; SPSS, Chicago, IL). The Kolmogorov-Smirnov test was used to confirm the assumption of normal distribution. In the event of biased data, a non-parametric test was applied. Data were presented using descriptive statistics, including frequency count and percentages for categorical data, and the median with interquartile range for continuous data. A non-parametric Kruskal-Wallis test compared continuous variables (median and interquartile range), while cross-tabulation, a chi-square test, and Fisher's exact were used to compare categorical variables. All tests were two-sided, and a p-value <0.05 was considered significant.

RESULTS

Of the 2,141 patients assessed for eligibility, 1,984 were excluded because they did not receive high-dose gonadotropins. A total of 157 patients were identified as poor responders and included in the study (Figure 1). The patients' characteristics are presented in Table 1. There was no difference between the 4 treatment groups in terms of age, BMI, duration of infertility, and basal E2, PRL, and TSH levels. Median basal FSH was 7 mIU/mL in all groups except the rFSH + rLH group, in which the median was 8 mIU/mL (IQR: 7–12) ($p = 0.049$), and there was a statistically significant difference in basal LH among the treatment groups ($p = 0.007$).

The causes of infertility among the participants are presented in Table 2. Overall, male factor infertility was the most prevalent cause across the study population (33.1%). In Group 4 (hMG), the proportion of patients with polycystic ovary syndrome (PCOS) was 66.7% (2/3 patients). In Group 1 and Group 3, PCOS was not observed.

Among the causes classified as 'Multiple causes,' Group 3 (rFSH alone) accounted for 11.8% (2/17). Nevertheless, no significant differences were observed among the four groups with respect to the other causes of infertility.

The duration of treatment, final E2 level, number of follicles of 16 mm, number of follicles of 11-15 mm, number of oocytes, number of frozen embryos, number of inseminated ICSI oocytes, and number of frozen ICSI oocytes, did not differ significantly between the four treatment groups. There was, however, a significant difference in total doses between groups, with rFSH + LH having the highest dose, at 600 IU/day (450-600) (Table 3).

Rates of positive pregnancy tests, live births, clinical pregnancy, and implantation showed no significant differences between the four groups.

Forty-three patients had a previous history of miscarriage; there was a significant difference between the groups, with the highest percentage (48.8%) in the hMG group (P = 0.046).

Among the 157 patients, 19 had their cycles cancelled for various reasons, and 21 had all of their embryos frozen; of the latter, the highest proportion (12 patients) were from the hMG group. One hundred thirty-five patients had an embryo transfer. Of the 53 (39.26%) patients who had positive pregnancy tests, 9 had a biochemical pregnancy, which was highest among the hMG group. Of the 53 patients with positive pregnancy tests, 44 (83.0%) continued to clinical pregnancy, resulting in 28 live births and 11 miscarriages, with 5 losses occurring prior to confirmed clinical pregnancy. In the current cycles, there were no ectopic pregnancies among our sample. Of the 135 patients who underwent embryo transfer, 25 had a 50% implantation rate: 4 (16.0%) were from the rFSH+LH, 7 (28.0%) from the rFSH+hMG group, 3 (12.0%) from the rFSH group, and 11 (44.0%) from the hMG group. Only 4 patients had a 100% implantation rate: 2 (50.0%) from the rFSH group and one each (25%) from the rFSH+LH and the hMG groups (Table 4).

The highest number of live births occurred in the 35—39 and ≥ 40 years age groups with equal proportions in each (n = 11/28, 39.3%). The incidence of live births in the < 35 year age group was 6 (21.4%) of the total pregnancies, among which 2 (28.6%) were from the rFSH + hMG group (n=7), 2 (33.4%) from the rFSH group (n=6), and 2 (22.2%) from the hMG (n=9) group. The highest number of live births according to group occurred in the hMG treatment group (n = 9/28, 32.1%). There was no statistically significant association between age and treatment groups concerning the number of live births (p = 0.553) (Table 5).

DISCUSSION

In this study, we sought to compare the relative effectiveness of four protocols for improving ovarian response and pregnancy rates in poor responders undergoing COH prior to IVF/ICSI under a GnRH antagonist protocol. Our findings revealed a significant difference between the groups in the total dose of gonadotropins per treatment; this is in contrast to the results of a meta-analysis of randomized clinical trials that showed no statistically significant difference in rFSH doses between groups (95% CI: 64–296) [16].

Our results showed that among those who had a positive pregnancy test, 11 patients suffered a miscarriage: the highest percentage was from the rFSH+LH group, although this finding was not statistically significant. Conversely, a meta-analysis conducted by Mochtar et al. showed favorable use of rLH with rFSH to decrease spontaneous miscarriages; this finding was also not statistically significant (seven trials: OR 0.57; 95% CI: 0.33—1.00) [16].

In a recent meta-analysis of 40 randomized controlled studies, more oocytes were retrieved, and significantly higher clinical pregnancy rates achieved, with the addition of rLH to rFSH versus rFSH alone in poor responders [17]. This finding was not supported by our results, which showed no difference in the rate of clinical pregnancies or

number of oocytes retrieved between the four groups. Another meta-analysis of randomized controlled clinical trials (RCTs), in which GnRH antagonists were used for pituitary suppression, found no significant differences in terms of clinical pregnancy rates; none of these studies reported live birth rates [18]. This was consistent with our results, which showed no statistically significant difference in the rate of live births or clinical pregnancies between the groups. However, although the live birth rate was highest in the hMG group (9.4%) compared with the other groups, even a small increase in percentage may be clinically relevant and should be interpreted with caution, as a lack of statistical significance does not always imply a lack of clinical significance.

Our study found no statistically significant difference in live birth rates between the four treatment groups after stratifying the patients according to age. In contrast, a previous retrospective study among poor responders found an extremely low cumulative live birth rate per oocyte retrieval cycle (2.7%) and per patient (6.1%) in those aged 40—50 years [19]. Likewise, another study concluded that live birth rates decreased significantly with increasing age ($P < 0.001$) [19]. Moreover, the same study showed that for women younger than 31 years who used the freeze-all strategy, the live birth rate for the first complete cycle was 63.81% (95% CI: 62.80–64.80%); this decreased substantially to 4.71% (95% CI: 3.61–6.02%) for women over 40 years [19]. An RCT including 749 women reported that highly purified hMG is at least as effective as rFSH in GnRH antagonist cycles, in terms of live birth rate (40% vs. 38%) [20]. According to the best available evidence, the addition of rLH to rFSH results in similar live birth rates compared with rFSH alone [21]. Another meta-analysis of 12 RCTs demonstrated that the probability of a live birth following treatment with hMG was significantly higher in comparison with r-FSH [OR = 1.20; 95% CI: 1.01–1.42] [22]. Additionally, a different RCT among 140 patients found that live birth rates and clinical pregnancy rates were higher in the rFSH+hMG group than in the rFSH+LH group ($p < 0.05$) [23].

The results might imply that a combination of gonadotropins is superior to a single gonadotropin in poor responders. This may be reflected through the number of oocytes retrieved and fertilized, the number of embryos transferred, and, ultimately, the number of live births, which is the ultimate objective of the ART cycle. However, there remain unquantifiable biases and other confounding factors that can be overlooked in such comparisons, such as the embryo culture, the endometrial lining, and other factors.

To the best of our knowledge, this is the first study to compare these four treatment protocols specifically in poor responders in the Middle East and North Africa (MENA) region. Nevertheless, due to its retrospective nature and the broad age group, biases may exist. Another limitation is that patients were recruited from a single center, which may limit generalizability to different populations. A robust database is needed to monitor any differences between these groups in terms of reproductive outcomes. Future studies are of great importance to investigate the need for high doses of gonadotropins in poor responders, to emphasize any safety issues among this patient group, and to consider the complexity of their treatment which may require a better-tailored protocol for patients with POR. There is a still great need for an assisted reproductive technology registry in Saudi Arabia that can facilitate data comparison between individual Saudi Arabian centers and international registries.

CONCLUSION

This study compared the effectiveness of high-dose gonadotropins on reproductive outcomes in poor responders. We found a significant difference in the total dose of gonadotropins per

cycle between the four treatment groups; however, increasing the total dose per day was not associated with any statistical difference in reproductive outcomes. This raises the question of whether subjecting patients to such high doses of gonadotropins is necessary or clinically justified. Future studies should focus on determining the optimal treatment options for this patient population.

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Appendix

Table 1. Demographics and Clinical Characteristics of Study Participants

Variable	Group 1 rFSH + rLH (n=29)	Group 2 rFSH + hMG (n=38)	Group 3 rFSH (n=20)	Group 4 hMG (n=70)	P-value
Age (yrs)	39.5 (34-41)	35 (32-39)	35.50 (31.50-38.50)	39 (36-41)	0.119
BMI (kg/m2)	31 (28-33)	29 (26-32)	29 (25.5-31.50)	29 (27-33)	0.649
Duration of infertility (yrs)	7 (4-9)	7.50 (5-12)	6 (3-11)	6 (4-10)	0.502
Basal FSH (mIU/ml)	8 (7-12)	7 (6-9)	7 (4-10)	7 (5-8)	**0.049**
Basal LH (mIU/ml)	7 (5-24)	5 (4-6)	6 (4.50 - 8.50)	5.50 (4-8)	**0.007**
Basal E2 (pg/ml)	129 (50-269)	128 (63-207)	160 (91-368.50)	155.50 (93-264)	0.425
Basal PRL (ng/ml)	280 (153-355)	177 (11-389)	271 (143 - 406)	213 (37-378)	0.447
Basal TSH (µIU/ml)	2 (2-3)	2 (2-4)	3 (1.50 - 3)	2 (2-4)	0.881

Values are expressed as median (Q1-Q3), and significant variables are in bold.

Table 2. Causes of infertility among the four treatment groups

Variable	Group 1 rFSH + rLH (n=29)	Group 2 rFSH + hMG (n=38)	Group 3 rFSH (n=20)	Group 4 hMG (n=70)	P-value
Unexplained	4/20 (20.0)	5/20 (25.0)	1/20 (5.0)	10/20 (50.0)	0.833
Anovulation	8/45 (17.8)	16/45 (35.6)	4/45 (8.9)	17/45 (37.8)	0.19
Polycystic ovary syndrome	0/3 (0.0)	1/3 (33.3)	0/3 (0.0)	2/3 (66.7)	1
Tubal factors	3/12 (25.0)	2/12 (6.2)	0/12 (0.0)	7/12 (58.3)	0.487
Male factors	9/45 (20.0)	9/45 (20.0)	8/45 (17.8)	19/45 (42.2)	0.598
Multiple causes	4/17 (23.5)	4/17 (23.5)	2/17 (11.8)	7/17 (41.2)	0.963
Male/Female factors	6/27 (22.2)	6/27 (22.2)	6/27 (22.2)	9/27 (33.3)	0.221

Values are expressed as numbers and percentages, and significant variables are in bold.

Table 3. Clinical results among the different treatment groups

Variable	Group 1 rFSH + rLH (n=29)	Group 2 rFSH + hMG (n=38)	Group 3 rFSH (n=20)	Group 4 hMG (n=70)	P-value
Number of Follicles of 16 mm	2 (1-3)	2 (1-3)	2 (2-3)	2 (1-4)	0.912
Number of Follicles of 11-15 mm	4 (2-6)	5 (2-7)	3 (2-5)	3(1-5)	0.215
Total daily treatment dose (IU)	600 (450-600)	450 (450- 450)	300 (300-375)	412.50 (300-450)	0.001
Duration of treatment (days)	10 (9-16)	10 (9-12)	10.50 (9-13)	10 (9-12)	0.807
Total gonadotropin dose (IU/cycle)	2250.50 (1350-3375)	2025 (1575-3150)	1762 (1350-3337.50)	2100 (1437-3750)	0.943
E2 level on hCG day (pg/ml)	4106 (2000-5834)	4577.50 (3506-6218)	4765.50 (1905.50-6584)	4099 (2131-6925)	0.835
LH level on hCG day (mIU/mL)	5 (2-10.90)	2 (1-3)	3 (1.65-3.50)	3 (2-4)	0.059
Number of oocytes collected	5 (2-8)	7 (3-12)	7 (4-10)	5.50 (2-8)	0.07
Number of embryos frozen	0	0	0	0	0.969
Number of ET	2 (1-2)	2 (1-2)	2 (1.50-2)	2 (1-2)	0.569
Number of inseminated ICSI	4 (2-5)	5 (2-8)	4.50 (3.50-7.50)	4 (2-6)	0.326
Number of frozen ICSI	3 (1-4)	4 (2-7)	3 (2-5)	3 (1-5)	0.216
ET day	3 (2-3)	3 (2-3)	3 (2-3)	3 (2-3)	0.187

Table 4. Reproductive outcomes of study participants

Variable	Group 1 rFSH + rLH (n=29)	Group 2 rFSH + hMG (n=38)	Group 3 rFSH (n=20)	Group 4 hMG (n=70)	P-value
Live births/cycle	6/28 (21.4)	7/28 (25.0)	6/28 (21.4)	9/28 (32)	0.338
Clinical pregnancy (total)	5/29 (17.2)	7/29 (24.1)	5/29 (17.2)	12/29 (41.4)	
Clinical pregnancy (single)	4/25 (16.0)	7/25 (28.0)	3/25 (12.0)	11/25 (44)	
Clinical pregnancy (twin)	1/4 (25.0)	0/4 (0.0)	2/4 (50.0)	1/4 (25.0)	0.199
Positive pregnancy test	11/53 (20.8)	11/53 (20.8)	8/53 (15.1)	23/53 (43.4)	0.803
Parity	3/27 (11.1)	7/27(25.9)	1/27 (3.7)	16/27 (59.3)	0.223
History of miscarriage	10/43 (23.3)	4/43 (9.3)	8/43 (18.6)	21/43 (48.8)	**0.046**
History of ectopic pregnancy	3/9 (33.3)	2/9 (22.2)	0/9 (0.0)	4/9 (44.4)	0.55
Miscarriage	5/11 (45.5)	2/11 (18.2)	1/11 (9.1)	3/11 (27.3)	0.177
Cancelled cycle	3/19 (15.8)	4/19 (21.1)	2/19 (10.5)	10/19 (52.6)	0.953
No. of eggs collected	0/6 (0.0)	2/6 (33.3)	1/6 (16.7)	3/6(50.0)	0.727
Froze all embryos	4/21 (19.0)	4/21 (19.0)	1/21 (4.8)	12/21 (57.1)	0.544
No fertilization	0/9 (0.0)	1/9 (11.1)	0/9 (0.0)	8/9 (88.9)	0.073
Negative pregnancy test	12/63 (19.0)	17/63 (27.0)	10/63 (15.9)	24/63 (38.1)	0.54
Converted to IUI	1/9 (11.1)	2/9 (22.2)	1/9 (11.1)	5/9 (55.6)	0.959

Values are expressed as numbers and percentages, and significant variables are in bold.

IUI: Intrauterine Insemination

Table 5. Distribution of Live births by Age Group and Treatment Groups

Age Group	Group 1 rFSH +LH (n = 6)	Group 2 rFSH + hMG (n = 7)	Group 3 rFSH (n = 6)	Group 4 hMG (n = 9)	Total (n = 28)	p-value
< 30 yrs.	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (3.6)	0.553
30-34 yrs.	0 (0.0)	2 (28.6)	1 (16.7)	2 (22.2)	5 (16.7)	
35-39 yrs.	2 (33.3)	3 (42.8)	3 (50.0)	3 (33.3)	11 (39.3)	
≥ 40 yrs.	4 (66.7)	2 (28.6)	1 (16.6)	4 (44.5)	11 (39.3)	

Numbers in parentheses are in percentages, and significant variables are in bold.

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