Effect of HMG on Pregnancy Outcomes in Patients undergoing IUI Cycle -An Analysis of 1230 IUI Cycles

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Research Article

Keywords: pregnancy rate, live birth rate, intrauterine insemination, human menopause gonadotropin, infertility

Posted Date: May 6th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-448689/v1

Abstract

Background: This aim of this study was to evaluate the effect of human menopause gonadotropin (HMG) on pregnancy outcomes of infertility patients with intrauterine insemination (IUI) treatments.

Methods: This retrospective cohort study analyzed couples using 75 IU HMG as initiate ovarian stimulation method for IUI from January 2015 to December 2019. Couples were divided into four groups according to a total dose of HMG: 189 cycles with a dose <500 IU, 601 with a dose 500 to1000 IU, 199 with a dose 1000 to 1500 IU and 241 with a dose ≥1500 IU. The differences in baseline characteristics and pregnancy outcomes including among the four groups were investigated. We used a logistic regression model to further study the association between various doses of HMG and pregnancy outcomes and adjusted for confounding factors.

Results: The study included 792 couples with 1230 cycles, and pregnancy was achieved in 212 (17.2%) cycles, while live birth was achieved in 176 (14.3%) cycles. Stratified analyses revealed that a higher dose of HMG was associated with increased pregnancy rate (PR), live birth rate (LBR), endometrial thickness (EMT) on insemination day, number of follicle ≥18 mm, serum estrogen 2(E2) level, and EMT on the trigger day among four groups, which were all statistically different (P<0.05). The logistic regression indicated that both PR and LBR were positively associated with the total dose and day of HMG, which were statistically different (P<0.05).

Conclusion: Increasing the total dose and day of HMG may benefit the serum E2 level, EMT, follicle development, and pregnancy outcomes in 75IU HMG stimulated IUI cycles.

Introduction

Globally, 10–15% of reproductive-age couples suffer from infertility, which is regarded as a public health phenomenon by World Health Organization (WHO) [1]. According to European Society of Human Reproduction and Embryology (ESHRE), nearly 776,000 assisted reproductive technology (ART) cycles and 175,000 intrauterine insemination (IUI) cycles were performed in Europe each year [2]. The higher incidence of cancer and congenital disability observed during the in vitro fertilization (IVF) cycles reminds us of careful consideration [3–5]. IUI, a safe and relatively low-cost procedure, is often the first-line in infertility treatment for couples with unexplained infertility, low-grade endometriosis, sexual function disorders, and low-grade male subfertility [6]. The pregnancy rate (PR) following IUI varies from 5 to 54.3%, which approaches IVF cycle [7]. Given the high cost and adverse offspring outcome of IVF, optimizing the strategies to improve IUI pregnancy outcomes is critical. Compared with natural cycles, ovarian stimulation with IUI therapy contributes to better PR [8].

Gonadotropin, a glycoprotein hormone that regulates both the development of gonad and the production of sex hormone, can stimulate follicular growth and endometrial development [9]. Studies revealed that gonadotropin led to a higher PR than tablets stimulated cycles such as clomiphene and letrozole [10–11]. Live birth rate (LBR) was found to reach 52% in women with normogonadotropic anovulation allocated to

gonadotrophin in six cycles [7]. Human menopause gonadotropin (HMG), one of the most widely used gonadotropin products, is extracted from menopause women's urine which can effectively induce follicle and endometrial development. The risks of ovarian hyper-stimulation syndrome (OHSS) and multiple pregnancies could be minimized with appropriate HMG dose and rigorous ultrasound monitoring of follicular development [12].

However, there is no consensus in the current literature regarding the specific association between HMG and pregnancy outcomes during HMG-stimulated IUI cycles. Therefore, to demonstrate a more accurate relationship between total HMG dose and pregnancy outcomes during IUI cycles, we compared the factors that optimize IUI outcome.

Materials And Methods

Participants

Using electronically extracted retrospective data from an infertility center in China during January 2015 and December 2019, we investigated all IUI cycles, including 2,290 cycles and 1,326 patients. Women were included if they fulfilled all of the following criteria: (i) couples diagnosed as infertility, defined as failing to conceive after 12 months of attempting conception; (ii) age 20–40 years; (iii) normal tubal patency as diagnosed by hysterosalpingography or laparoscope, normal uterine and endometrial as diagnosed by ultrasound or hysteroscopy in past 12 months; (iv) a minimum of 10 million motile sperm cells/milliliter (mL) after washing; (v) women stimulated with an initial dose of 75 IU HMG, and patients with medical conditions that are contraindicated to IUI procedures or pregnancy, such as poorly controlled hypertension or diabetes, undiagnosed organ disease, history of thrombosis or cancer. The trial was approved by the ethics committees of the institutional review board of the Third Affiliated Hospital of Guangzhou Medical University. All the couples, including female and male partners, provided written informed consent.

Ovulation Induction and Sperm Preparation Protocols

Basic characteristics including age, BMI, anti-Müllerian hormone (AMH), semen analysis of husband were all assessed before IUI cycles. Administration of 75 IU HMG started on day 2 to day 5 of the cycle, while the day and dose of HMG were adjusted according to follicles' development with serum estradiol level and ultrasound monitoring. Ovulation was triggered with 8,000 IU of human chorionic gonadotropin (hCG) when the luteinizing hormone (LH) peak increased, or the lead follicle diameter reached 18-20 mm. The number of preovulatory follicles with more than 18 mm diameter, endometrial thickness (EMT), serum E2 levels on the trigger day, and EMT on the insemination day were recorded. Insemination was carried out 0 to 36 hours after triggering, and cycles with more than three preovulatory follicles were canceled.

All semen specimens were prepared by a gradient technique obtained by masturbation into sterilized containers after 2-7 days of abstinence, processed with a two-layer density gradient liquefied for 20-30 minutes at room temperature [13]. Semina morphology, including motility, volume, and count, was

assessed according to WHO guidelines [14]. A soft catheter was used to inject 0.3 to 0.5 mL of the selective semen specimen into the uterine cavity. Females were required to maintain a supine position for 20 minutes after insemination.

Luteal progesterone supplementation was routinely prescribed to all patients up to the day of the hCG test and would be continued until the eighth week of gestation if the hCG test was positive. Serum hCG measurement was tested 14 days after insemination, and a gestational sac detection by transvaginal ultrasound was performed after four weeks of insemination if the hCG test was positive. The main outcome was pregnancy which is defined as the positive test of hCG. Live birth was defined as delivery with a gestational age of ≥28 weeks.

Statistical analysis

Analyses were performed for PR and LBR. First, the factors between pregnancy and nonpregnancy, live birth, and non-live birth, were compared. Second, features among four groups of different doses were further explored. Categoric variables, expressed as number of cases (n) with occurrence percentage (%), were compared among the groups utilizing chi-square ($x2$) or Fisher exact tests. Continuous variables, expressed as mean±SD, were analyzed using analysis of variance (ANOVA) or Student t-test. The normality of continuous variables was assessed using Shapiro-Wilk normality test. Thirdly, PR and LBR per IUI cycle were plotted against the total dose and day of HMG in increments of 1 mm. Finally, bivariate logistic regression analysis was used to assess whether any of the following variables could explain PR and LBR: female age, male age, AMH of female, progressive sperm of male, infertility duration initial day, total dose, and day of HMG. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for associations between HMG, PR, and LBR were calculated. All calculated P values were two-sided, and P values less than 0.05 were considered statistically significant. All statistical analyses were performed with SPSS version 26 and GraphPad Prism 8.

Results

Of the 2,290 cycles recorded in the infertility medical data from January 2015 to December 2019, 1230 cycles for 792 couples were available for this analysis after excluding inadequate age, different ovulation treatment, and initiating dose. Demographic characteristics of all participants by PR and LBR are shown in Table 1. PR and LBR were 17.8% and 14.3%, respectively. The couples who failed to get pregnancy or delivery were statistically significantly older and had a longer infertility duration ($P < 0.05$). The progressive motility sperms of males and AMH of females tend to be better in those with pregnancy and live birth. No statistically significant differences were found regarding body mass index (BMI), infertility indication, number of IUI cycles, total sperm volume, and total sperm concentration between couples with pregnancy or who gave birth and those who failed. No case of OHSS was recorded among these couples.

Table 1
Baseline characteristics of the population

		Pregnancy			Live birth		
	All	positive (n = 212)	negative (n = 1018)	*p* Value	positive (n = 176)	negative (n = 1050)	*p* Value
Female Age (years)	31.65 ± 3.94	31.00 ± 3.98	31.78 ± 3.92	0.008	30.91 ± 3.91	31.77 ± 3.91	0.007
Female BMI **(kg/m^2)**	21.89 ± 10.00	21.69 ± 2.94	21.93 ± 1.90	0.751	21.70 ± 2.96	21.92 ± 10.73	0.785
AMH (ng/ml)	5.75 ± 4.44	6.47 ± 5.10	5.60 ± 4.28	0.064	5.90 ± 4.21	5.73 ± 4.48	0.750
Male Age (years)	33.67 ± 4.84	32.96 ± 4.89	33.82 ± 4.83	0.018	32.84 ± 4.98	33.81 ± 4.81	0.013
Male BMI **(kg/m^2)**	23.77 ± 3.55	24.13 ± 3.76	23.69 ± 3.50	0.140	24.07 ± 3.75	23.72 ± 3.51	0.271
total sperm count (ml)	3.32 ± 1.50	3.35 ± 1.27	3.31 ± 1.55	0.775	3.35 ± 1.26	3.31 ± 1.54	0.794
Total sperm concentration (10^6/ml)	45.73 ± 30.14	48.41 ± 31.32	45.18 ± 29.87	0.155	48.65 ± 32.08	45.25 ± 29.80	0.166
Progressive motility sperms (%)	49.84 ± 18.55	51.97 ± 17.86	49.38 ± 18.68	0.097	52.83 ± 17.27	49.74 ± 18.55	0.037
Number of IUI cycles	1.89 ± 1.00	1.80 ± 0.92	1.9 ± 1.02	0.163	1.78 ± 0.92	1.91 ± 1.02	0.155
Primary infertility		52.4%	55.4%	0.418	54.9%	54.4%	0.924
Infertility duration	3.16 ± 2.17	2.81 ± 1.91	3.24 ± 2.21	0.009	2.77 ± 1.95	3.23 ± 2.19	0.008
Indication for IUI	0.962				0.782		
Female factor		23.1%	24.0%		24.2%	21.6%	0.782
Male factor		32.5%	33.0%		32.6%	34.7%	
Both factor		3.3%	3.7%		3.8%	2.8%	
Unexplained		41%	39.3%		39.4%	40.9%	
Total day of gonadotropins (day)	10.46 ± 4.37	11.60 ± 4.94	10.22 ± 4.21	0.000	11.35 ± 4.67	10.31 ± 4.31	0.003

		Pregnancy			Live birth		
Total dose of gonadotropins (IU)	1078.76 ± 838.89	1277.66 ± 991.73	1037.34 ± 797.75	0.000	1225.57 ± 924.57	1054.25 ± 821.63	0.012
Initial day of menstrual	4.39 ± 2.34	4.43 ± 2.34	4.38 ± 2.34	0.054	4.39 ± 2.12	4.39 ± 2.37	0.991
No. of follicles>18mm	0.08				0.081		
0	35.4%	34.1%	35.7%		32.9%	35.9%	
1	45.9%	39.2%	47.3%		41.8%	46.6%	
2	18.7%	26.7%	17.0%		25.3%	17.5%	
E2 on day of trigger (pmol/ml)	2372.87 ± 1574.57	2344.85 ± 1477.67	2324.48 ± 15959.08	0.996	2295.784 ± 1433.45	2385.754 ± 1695.17	0.541
EMT of trigger day(mm)	9.41 ± 1.63	9.61 ± 1.60	9.37 ± 1.64	0.079	9.65 ± 1.70	9.37 ± 1.63	0.086
EMT on day of insemination (mm)	9.82 ± 2.43	9.94 ± 1.51	9.79 ± 2.58	0.46	9.88 ± 1.53	9.81 ± 2.55	0.74

BMI: body mass index; AMH: anti-müllerian hormone; IUI: intrauterine insemination; HMG: human menopause gonadotropin; E2: estrogen; EMT: endometrial thickness

As shown in Table 1, the mean dose of women treated with HMG was 1078.02 ± 838.83 IU, among those with pregnancy and who gave birth were 1277.66 ± 991.73 and 1225.57 ± 924.57 IU and among those who failed were 1037.34 ± 797.75 and 1054.25 ± 821.63 IU, which were both statistically significant (P< 0.05). To explore the effect of different HMG doses on pregnancy outcomes, couples were divided into four groups according to HMG dose distribution: Group A, < 500 IU, Group B, 500 to1000 IU, Group C, 1000 to 1500 IU, and Group D,>1500 IU. The comparison of baseline characteristics of participants in the four HMG groups is displayed in Table 2. Those women who cost a higher HMG were younger and had a higher AMH level, which were both statistically significant (P< 0.05). The progressive motility sperms of males were higher with a higher HMG dose of their partners. The total day of HMG was significantly longer as the dose of HMG accumulated higher (P < 0.05). The differences among other baseline characteristics were nonsense (P>0.05).

Table 2
Comparison of 4 groups of different dose of HMG administered

	Group A	Group B	Group C	Group D	F/$\chi 2$	p Value
	<500IU (n = 189)	500-999IU (n = 601)	999-1455IU (n = 199)	≥ 1500(n = 241)		
Female age (year)	32.06 ± 3.86	31.81 ± 3.87	31.81 ± 4.03	31.32 ± 4.15	2.787	0.040
Female BMI (kg/m^2)	20.73 ± 13.91	21.90 ± 13.91	22.344 ± 11.96	22.89 ± 3.52	1.411	0.238
AMH (ng/ml)	4.25 ± 2.97	5.33 ± 4.01	6.67 ± 5.49	6.68 ± 4.68	7.828	0.000
Male age (year)	34.17 ± 4.86	33.74 ± 4.62	33.60 ± 4.93	33.42 ± 5.20	2.194	0.087
Number of IUI cycles	1.96 ± 1.00	1.90 ± 1.02	1.83 ± 0.93	1.84 ± 1.06	0.561	0.641
Infertility duration(year)	3.05 ± 2.16	3.08 ± 2.23	3.20 ± 2.23	3.19 ± 2.04	0.473	0.701
Indication for IUI					13.616	0.137
Female factor	29.6%	23%	23.1%	22.1%		
Male factor	23.3%	34.3%	38.7%	32.5%		
Both factor	4.8%	3.5%	3.5%	3.3%		
Unexplained	42.3%	39.3%	34.7%	42.1%		
Initial day of menstrual	5.47 ± 3.58	4.44 ± 2.17	3.93 ± 1.42	3.83 ± 1.89	15.68	0.000
Total dose of HMG (IU)	381.15 ± 175.79	702.96 ± 132.41	1268.99 ± 144.62	2405.92 ± 1001.24	970.19	0.000
Total day of HMG	5.12 ± 0.97	9.06 ± 1.68	12.24 ± 2.25	16.68 ± 4.14	965.151	0.000
total sperm count (ml)	3.33 ± 1.51	3.31 ± 1.53	3.41 ± 1.44	3.23 ± 1.50	0.430	0.732
Total sperm concentration (10^6/ml)	47.00 ± 32.64	45.48 ± 29.64	48.54 ± 33.23	42.55 ± 26.15	1.585	0.191
Progressive motility sperms (%)	46.12 ± 19.25	49.89 ± 18.83	50.96 ± 17.87	51.42 ± 17.75	2.720	0.043

HMG: human menopause gonadotropin; BMI: body mass index; AMH: anti-müllerian hormone; IUI: intrauterine insemination

As demonstrated in Table 3, when ovaries were stimulated with higher HMG dose, EMT on day of trigger and insemination, the mean number of follicles bigger than 18 mm, and the level of serum E2 were all increased significantly (P < 0.05). PR and LBR were significantly higher in high dose groups which were 11.3%, 15.5%, 18.1 % and 25.8 %, 9.5%, 13.6%, 14.1% and 20.0%, respectively ($P < 0.05$).

Table 3
Comparison of outcomes among 4 groups of different dose of HMG administered

	Group A	Group B	Group C	Group D	F/χ2	*p* Value
	<500IU (n = 189)	500-999IU (n = 601)	999-1455IU (n = 199)	≥ 1500(n = 241)		
Pregnancy rate	11.1.% (21)	15.5% (93)	18.1% (36)	25.8% (62)	18.803	0.000
Live birth rate	9.5% (18)	13.6% (82)	14.1(28)	20.0(48)	10.08	0.018
E2 on day of trigger	1874.66 ± 1187.20	2259.53 ± 1547.80	2881.60 ± 1850.47	3121.08 ± 2212.38	7.742	0.00
No. of follicle ≥ 18mm on the day of trigger					62.778	0.000
0	38.3%	30%	37.6%	43.2%		
1	57%	53.2%	38.8%	28.6%		
2	4.7%	16.8%	23.5%	28.2%		
EMT on day of trigger(mm)	9.05 ± 1.6	9.3 ± 1.64	9.73 ± 1.56	9.74 ± 1.66	7.770	0.000
EMT on day of insemination (mm)	9.44 ± 1.61	9.68 ± 1.63	10.03 ± 1.35	10.33 ± 4.47	5.564	0.001
E2: estrogen; EMT: endometrial thickness						

According to HMG dose, PR and LBR distributions were displayed in Fig. 2, in which PR and LBR become higher as the dose becomes higher. Bivariate logistic regression was conducted to explore the possible factors that influenced PR and LBR. As shown in Table 4, results revealed a positive relationship between HMG dose or HMG day, with PR and LBR, which were all statistically different ($P < 0.05$). Adjusting the variables that affect pregnancy, including couple's age, infertility duration, AMH, progressive motility sperms, the initial day of menstrual and total day of HMG, did not change the results of the association mentioned above. The odds of PR at group 4 were 21.87%, 11.51%, and 5.07% higher than groups 1, 2, and 3, respectively. Simultaneously, the odds of LBR increased by 33.82%, 15.54%, and 8.7% compared to groups 1, 2, and 3, respectively. Both of odds were significantly different ($P < 0.05$)

Discussion

The primary objective of the present research was to discuss the relationship between pregnancy outcomes and total dose of HMG in couples undergoing HMG-stimulated IUI cycles with 75 IU as the initial dose. Analysis of 1,230 HMG-stimulated IUI cycles indicated that higher PR and LBR were associated with increasing HMG dose, and higher PR was also linked to enhancing HMG day after adjusting for potential confounders. These results suggest that increasing HMG dose appropriately would optimize PR and LBR of patients in HMG-stimulated IUI cycles, and longer days of stimulation cycle should not be abolished.

Using gonadotropin stimulated in IUI cycles has been widespread [1]. PR and LBR of each gonadotropin cycle, higher than oral ovulation drugs, were reported as 6.9–16.9% and 9.1–20.5%, respectively, consistent with our study [15]. Daily injection of appropriate doses of gonadotropins, an efficient and convenient treatment to mimic pulsatile gonadotropin-releasing hormone stimulation and normal ovarian function, could induce physiologic follicle development, normal estrogen level, appropriate EMT, and natural luteal function [16]. Both follicle-stimulating hormone (FSH) and LH are primary hormones for follicle development and maturation, fertilization ability of oocyte, and endometrium implantation capacity. According to a two-cell two-gonadotropin theory model, LH provides the major drive to thecal androgen synthesis, which is the substrate for FSH-induced estrogen synthesis in granulosa cells [17]. FSH leads to follicle growth, estrogen concentration, and endometrial proliferation. LH actives embryogenesis, meiotic division, and follicular wall proteolysis, which releases the oocyte [18]. LH was also believed to furnish appropriately estrogenic environment for normal follicular ontogeny, decrease development of small follicles, and optimize dominant follicle selection, alleviating risks of OHSS and multiple pregnancies [19]. Urine human menopausal gonadotropin (HMG), the combination of FSH and LH, is a low-cost and efficient ovulation medicine used in IUI cycles [20]. Earlier initial days and longer usage days of HMG were connected with a higher HMG dose in this study, which was meaningless after adjustment, indicating that HMG dose might be the essential factor in HMG-stimulated IUI cycles.

One of the considered mechanisms leading to high PR and LBR is the augment of E_2. Our study manifested a positive relationship between postovulatory E2 level and HMG dose, consistent with the two-cell two-gonadotropin theory that both FSH and LH regulate estrogen production. Increased circulating high E_2 released by follicles stimulates GnRH receptor expression in the pituitary gland, which then stimulates LH and follicle release [16]. Previous literature showed that infertility females with higher E_2 levels during the whole cycle were tended to have better chances of being pregnant [21]. The embryos with a higher E_2 level would obtain a better quality and development dynamics during in vitro fertilization [22]. Exogenous hormone experiment also showed that a gradual and constant augmentation, instead of a rapid increase, in the thickness of the endometrium stimulated by circulating estrogen was more likely to induce vasodilation and endometrial blood flow and increase the endometrial size during periovulatory periods, explaining why longer days of HMG were related to a better pregnancy outcome [23]. However, supraphysiologic estradiol levels are deemed to adversely affect endometrial receptivity and thereby implantation, resulting in an increased perinatal risk [24]. Consequently, physiologic estradiol level is required in IUI cycles. In the 75 IU HMG-stimulated cycle, no OHSS case was reported because follicles

number was controlled, and the estradiol level remained at an adaptive level which might be explained by the low initial dose of HMG.

The improvement of endometrial proliferation and receptivity, one of the most essential processes in successful mammalian implantation, may be another reason for the association between higher dose, longer days of HMG, and superior outcomes [17]. Many studies have explored the relationship between EMT and pregnancy outcomes in IUI and IVF treatments, but the consensus in the existing studies is inconsistent at best [20, 23]. Overall, most literature has shown that better pregnancy outcomes are observed with increasing EMT, which is in line with our results. For example, a study showed that within gonadotropin treatment IUI cycles, the mean EMT in women achieving the outcome of live birth was greater than those who failed, and 12.2% of live births were observed in cycles with an EMT of more than 13 mm [25]. Quaas et al. stated a positive association between peak EMT and PR in the setting of gonadotropin cycles with a peak EMT as between 10.5 and 13.9 mm [26]. Another report concerned about 1005 IUI cycles showed an increasing thickness of endometrium and PR in letrozole plus HMG protocol compared with letrozole cycles [20]. However, a multicenter randomized controlled trial manifested that HMG cycles led to a significantly thicker endometrium compared to clomiphene citrate in IUI for unexplained subfertility without a consistent association between EMT and ongoing PR [27]. The contradiction above might be explained by the different scope of endometrium thickness compared in the study above, and the excessive EMT is detrimental to the mammalian implantation, which should be controlled within reasonable bounds.

The number of preovulatory follicles was also a crucial element in embryogenesis success. Our results indicated that a growing mean number of follicles was connected with increased HMG dose but limited to three. Gonadotropin cycles tend to access more follicles than oral treatment, including clomiphene citrate and letrozole [7, 25]. More follicles do have more opportunity to get fertilized, but excess follicles could not contribute to PR and LBR because synchronization among different follicles would damage the endometrial receptivity [15]. As a result, adverse pregnancy outcomes should be avoided by limiting the number of follicles. Clinicians most widely use low staring dosages such as 37.5 to 75 IU HMG to control follicle number and lower adverse pregnancy outcomes such as hyper-stimulation syndrome and multiple pregnancies, so we selected 75 IU as the initial unified dosage [15, 28]. With a low initial dose, HMG overdose could be avoided, and optimal number of follicles could be managed. Increasing the dose and day of HMG appropriately to trigger one dominant follicle, physiological dose of estrogen, and endometrial development would improve IUI outcome to advantage.

This study's salient strengths are sample size and inclusion of 75 IU dose as initial stimulated dose the first time. To date, there have been few reports examining the effect of dose and day of HMG on pregnancy outcomes. Simultaneously, we acknowledge the retrospective nature of the present study as a limitation, but the bias of influences of other variables on pregnancy outcomes was eliminated by recruiting patients in a strict inclusion and exclusion standard. A high-quality RCT concerning more significant pregnancy outcomes in future studies is warranted.

Conclusions

In summary, PR and LBR were positively associated with the total dose and day of HMG in patients stimulated with 75 IU HMG as initial dose for IUI cycles. Incremental EMT, serum estrogen level, and number of preovulatory follicles might be associated with higher usage dose of HMG administered. These findings suggest that appropriately higher dose and day of HMG can optimize PR and LBR in HMG-stimulated IUI cycles without growing risk of OHSS, and clinicians should pay attention to serum estrogen level, endometrium, and preovulatory follicle development.

Abbreviations

AMH: anti-Müllerian hormone; ANOVA: analysis of variance; ART: assisted reproductive technology; BMI: body mass index; CIs: confidence intervals; E2:estrogen 2; EMT: endometrial thickness; ESHRE: European Society of Human Reproduction and Embryology; FSH: follicle-stimulating hormone; HCG: human chorionic gonadotropin; HMG: human menopause gonadotropin; IUI: intrauterine insemination; IVF: in vitro fertilization; LBR: live birth rate; LH: luteinizing hormone; OHSS: ovarian hyper-stimulation syndrome; ORs: odds ratios; PR: pregnancy rate; WHO :World Health Organization.

Declarations

Ethical Approval and Consent to participate

The study was approved by the local institutional review board.

Consent for publication

Not applicable.

Availability of supporting data

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported in part by grants from Foundation for Distinguished Young Talents in Higher Education of Guangdong 2017KQCN165.

Authors' contributions

OMX conceived and drafted the manuscript. LH and MKC analyzed and interpreted the patient data. XP and LMX read and revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors would like to thank for Yuhong Zhang for data collecting.

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Table

Table 4 is not available with this version

Figures

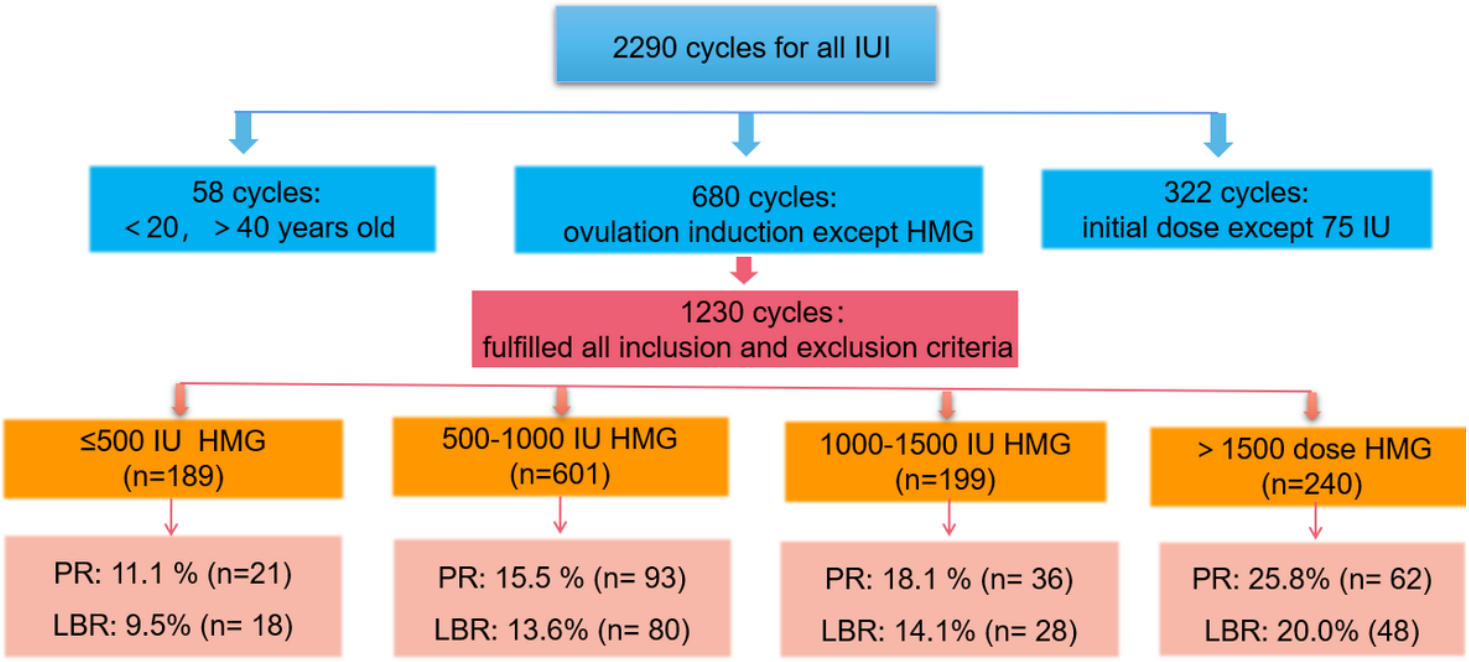
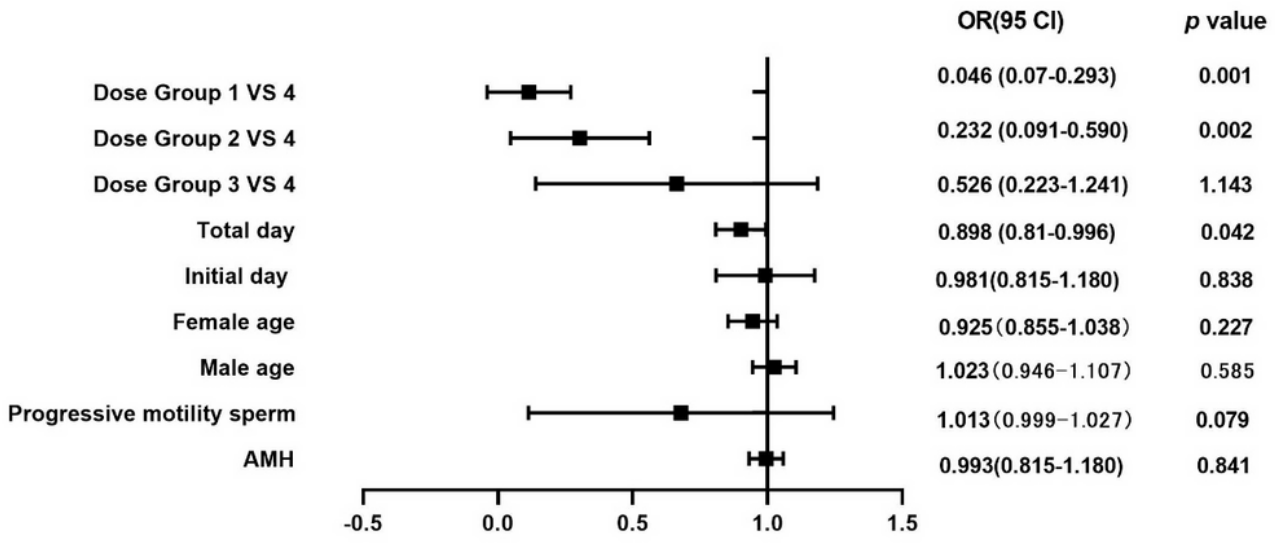
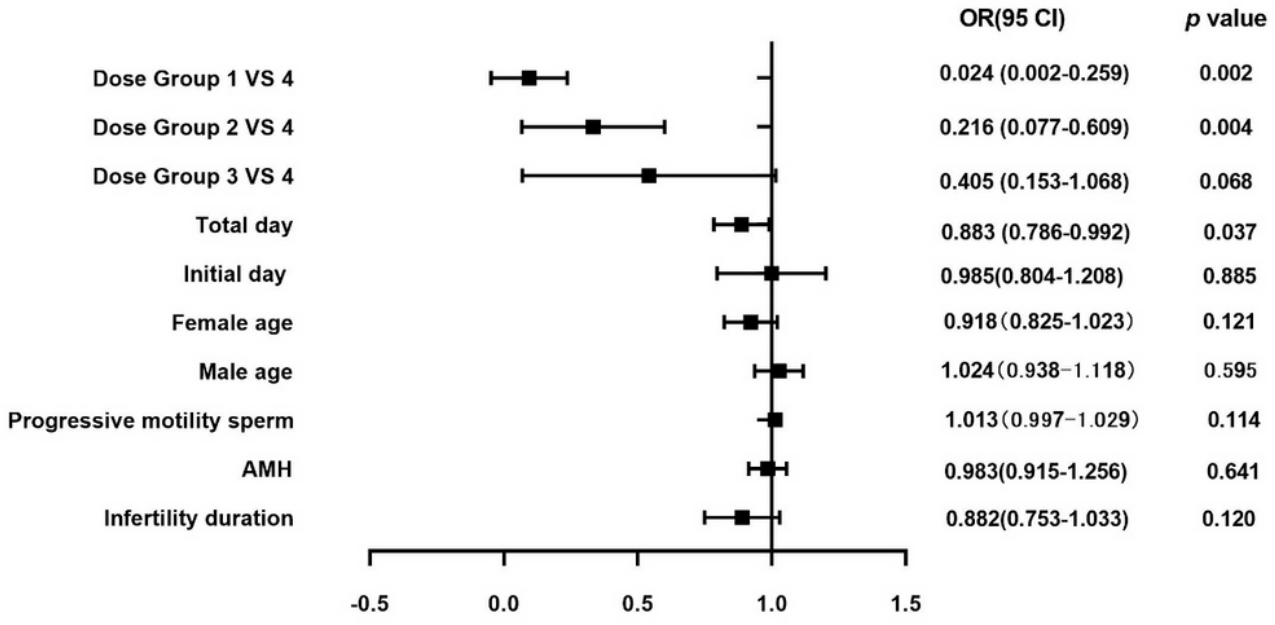


Figure 1

Pregnancy rate and live birth rate according to different total dose of HMG on IUI cycles



Variables associated with PR by logistic regression



Variables associated with LBR by logistic regression

Figure 2

Variables associated with dose of PR and LBR analyzed by logistic regression. PR: Pregnancy rate; LBR: live birth rate; OR, odds ratio; 95% CI, confidence interval.

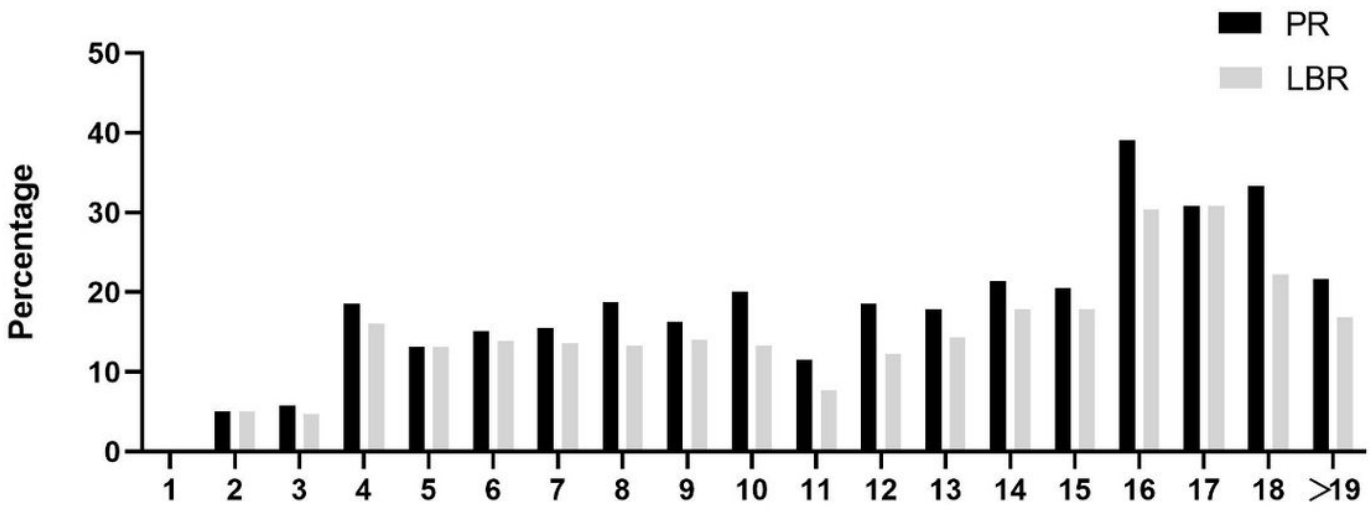


Figure 3

PR and LBR of the study cohort stratified by 100-IU increments of HMG