Original Article

Clinical Outcomes in Patients Receiving Originator Follitropin Alfa and Follitropin Alfa Biosimilars in Real-world Clinical Practice: A Retrospective Study

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Abstract

Background: Biosimilar drugs have broadened the treatment options in assisted reproductive technology (ART). Real-world data comparing clinical outcomes of originator follitropin alfa (Gonal-f®) with its biosimilars are required to enrich the body of evidence for clinical decision-making on choice of drug. **Aims:** To compare the ART outcomes in patients receiving originator follitropin (Gonal-f®) and its biosimilars in clinical setting. **Settings and Design:** Medical records of 364 infertile women who underwent ART between 2016 and 2020 at Akanksha Hospital and Research Institute, Gujrat, India, were retrospectively analysed. **Materials and Methods:** Participants were divided into two cohorts based on treatment (Gonal-f® cohort; $N = 174$ and biosimilar cohort; $N = 190$), each cohort further subdivided into group A (age <35 years) and group B (age ≥35 years). Fresh or frozen embryo transfer was performed as per the standard procedures of the clinic. Pregnancy rates and live birth rate (LBR) were the primary main outcome measures in this study. **Statistical Analysis Used:** Descriptive statistics and Chi-square test were used for analysis. **Results:** The number of oocytes retrieved from Gonal-f® and biosimilar cohorts were comparable (13.3 vs. 14.4). Compared to biosimilars, Gonal-f® treatment resulted in higher yield of cleavage stage and blastocyst stage embryos, and the proportion of women with good quality embryos was higher in the Gonal-f® cohort than the biosimilar cohort (83.3% vs. 69.5%). Patients receiving Gonal-f® reported higher pregnancy rates (59.2% vs. 39.7%) and LBR (43% vs. 17.7%) compared to those receiving biosimilars. **Conclusions:** Gonal-f® (originator follitropin) treatment could result in higher pregnancy rates and LBR in comparison to biosimilars in real-world setting.

Keywords: *Assisted reproductive technology, follitropin alfa, gonadotropin-releasing hormone antagonist, infertility*

Introduction

Gonadotropins are administered to induce ovulation and follicular stimulation as part of infertility treatment in women undergoing assisted reproductive technology (ART).[1] The availability and compatibility of follitropin alfa (Gonal-f®, Merck Healthcare KGaA, Darmstadt, Germany) and a variety of biosimilar recombinant human follicle stimulating hormone (r-hFSH) drugs have increased the choice of gonadotropins treatment option for healthcare practitioners and patients.[2] Live birth rate (LBR) is a widely recognised clinical indicator of ART along with pregnancy rates. Although previous studies have

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compared outcomes with Gonal-f® and its biosimilars, there is paucity in data on differences in reproductive outcomes and under real-world setting.[3-5] This study aims to fill the gap by comparing pregnancy outcome and LBR in patients receiving Gonal-f® or its biosimilars in a clinical setting.

Subjects and Methods

Study design

This was a retrospective, observational study that included 364 adult women with clinically diagnosed infertility undergoing ART at the Akanksha Hospital and Research Institute, a tertiary assisted-conception unit located in Anand, Gujarat, India, between 2016 and 2020. Data were collected and analysed from hospital medical records in this study. The study was approved by the Institutional Ethics Committee of Sat Kaival Hospital Pvt. Limited, Gujrat, India (reference number: EC/DHR/002/2023; EC registration number: EC/NEW/INST/GJ/0105). In view of use of anonymised data, the study was granted waiver of consent by the EC. The study was conducted in accordance with the Declaration of Helsinki (2013).[6]

Patient population

Medical records of all women (aged between 20 years and 50 years) diagnosed with infertility, selected by the anti-Müllerian hormone (AMH) and antral follicle count (AFC)-based screening procedures, and undergoing ART following ovarian stimulation with either originator follitropin alpha or biosimilars within the study period were included in the study. Women diagnosed with pregnancy, and those hypersensitive to gonadotropins were excluded. Patients were also excluded from the study if they had planned to undergo donor oocyte cycles, *in vitro* maturation cycles, and ovarian stimulation for preserving fertility. The study participants were divided into two cohorts based on administration of either Gonal-f® or its biosimilars. Affordability and advanced age of the patient were the two main criteria based on which the patients were assigned either to the Gonal-f® or the biosimilar cohorts. Each patient cohort was further divided into two subgroups based on the maternal age: group A (age <35 years) and group B (age >35 years).

ART protocol

ART was carried out using the standard gonadotropin-releasing hormone antagonist protocol in this study. Patients were screened by the AMH and AFC screening methods for ART. The process of ovarian stimulation was carried out with the originator r-hFSH, Gonal-f® (Merck Healthcare KGaA, Darmstadt, Germany), Folisurge [Intas Pharmaceutical], Newmon-R PFS™ [Cipla]. The patients received Gonal-f® (3099.042 IU) and biosimilars (2717 IU), based on age, AFC, AMH, and body mass index on day-1/day-2 of the menstrual cycle. The ovarian response to stimulation was monitored by serial follicle tracking using ultrasound scans.

Once the dominant follicles reached >14 mm diameter in size, an antagonist of gonadotropin-releasing hormone (GnRH) was injected, and was continued till the day of ovulation trigger. Doses of GnRH antagonist were adjusted primarily according to the size of the dominant follicle, and also on the number of dominant follicles. Trigger for ovulation, which consisted of either human chorionic gonadotropin (hCG) or GnRH agonist, or the combination of both hCG and agonist, was given to the patients when three or more follicles reached 18 mm of size. The ovum pick up procedure was performed 34 h post trigger using transvaginal sonography, under general anaesthesia.

Fertilisation was carried out by conventional *in vitro* fertilisation (IVF) or by intracytoplasmic sperm injection (ICSI) using partner's sperm, as per the standard procedure of the medical centre. The inseminated oocytes were examined after 16–18 h to assess the extent of fertilisation. Embryo transfers were performed using fresh embryos or frozen-thawed embryos. In case of fresh embryo transfer, micronised progesterone was administered intramuscularly at the dosage of 100 mg per day from the day of egg retrieval, for 3 days in case of cleavage-stage embryo transfer or for 5 days in blastocyst-stage embryo transfer. In case of frozen embryo transfer, the patient was put on hormone replacement therapy, which commenced from day-3 of menstrual cycle, with 2 mg of oral estradiol valerate or estradiol hemihydrate tablet, three times a day. When the optimal thickness of endometrium of 8 mm was reached, progesterone injection was administered at 100 mg/day, for 3 days in case of cleavage-stage or for 5 days in case of blastocyst-stage embryo transfer. Natural micronised progesterone was continued till the outcome date.

The number of embryos transferred in both cases, fresh or frozen, were a maximum of three cleavage-stage embryos or two blastocyst-stage embryos. Transfer of embryos was carried out using a soft embryo transfer catheter under ultrasound guidance. The sandwich method, also referred to as the air bubble method, was used to load the embryos using a catheter for embryo transfer. To confirm pregnancy, serum beta hCG was estimated 14 days after embryo transfer and viability was confirmed by ultrasound, 2 weeks after a positive beta hCG test.

Outcome measures

The key outcome measures included number of oocytes retrieved, number of embryos (both cleavage and blastocyst stage) on day 6, proportion of women with good quality of embryos, number of embryos transferred, clinical pregnancy rates, clinical miscarriage rates, and LBR.

Statistical analysis

Descriptive statistics were used to summarise the data and results reported as means and standard deviations (SDs), as applicable. Categorical variables were summarised as counts and percentages. Logistic regression analysis was performed to evaluate the likelihood of pregnancy rate, live-birth rate and miscarriage rate after treatment with Gonal-f® and its biosimilars, and was represented as odds ratios (ORs) with 95% confidence intervals (95% confidence interval [CI]). Comparison between two groups of continuous variables was carried out by an independent *t*-test, and Chi-square test was used for comparisons between categorical variables. *P* values were calculated and $P < 0.05$ was considered statistically significant. Missing data were not included in estimations of averages. Sample size calculation or power calculation has not been performed in this study. Data was entered using MS Excel software (Microsoft), and all statistical analyses were performed using SPSS statistical software package version 20.0 (IBM Corp., Armonk, New York).

Results

Baseline characteristics of the study population

In total, medical records of 364 infertile women undergoing ART were retrospectively analysed, with 174 and 190 patients in the Gonal-f® cohort and the biosimilar cohort, respectively. Subgroup analysis was performed based on age, where group A consisted of women <35 years, and group B consisted of women ≥35 years. The majority of the overall study population (234; 78%) consisted of patients in group A (<35 years of age).

Baseline characteristics of the patient population in this study are presented in Table 1. The mean age ± SD of patients ranged between 29.2 ± 3.3 and 37.5 ± 2.4 years. The demographic and baseline clinical characteristics between the patients of Gonal-f® and the biosimilar cohorts were comparable. Baseline levels of AMH (4.3 ng/mL vs. 5.4 ng/mL) and AFC were higher in patients of the biosimilar cohort compared to that of the Gonal-f® cohort. On the other hand, age (30.3 years vs. 29.2 years) and dosage of gonadotropin (2806.3 IU vs. 2618.8 IU) were relatively higher for patients of Gonal-f® cohort than the patients of the biosimilar cohort [Table 1].

The mean AFC ranged between 11.4 ± 4.8 and 13.9 ± 5.9 in the overall study population. Baseline treatment regimens included use of adjuvants such as growth hormone, estradiol and letrozole for the patients in this study.

The distribution of patients based on the method of fertilisation has been depicted in Figure 1. Both IVF and ICSI methods were used for fertilisation in majority of the patients of both the study cohorts as compared to IVF or ICSI alone, and patients of the Gonal-f® cohort had higher number of fertilisations by both IVF and ICSI compared to patients in the biosimilar cohort. In the Gonal-f® cohort, both IVF and ICSI were used in 73.5% of patients compared to 60% of patients in the biosimilar cohort. Only ICSI was used in similar proportion of patients (36%) in both Gonal-f® and biosimilar cohorts. Fertilisation only by IVF was used in least number of patients in both cohorts as compared to the other two methods, and was marginally higher in the biosimilar cohort compared to the Gonal-f® cohort [Figure 1].

Ovarian stimulation and embryological outcomes

The cycle characteristics are presented in Table 2. Although the mean number of oocytes retrieved was comparable between the biosimilars and Gonal-f® cohorts, the number was marginally higher in the biosimilar cohort (13.2 vs. 14.4). There was a difference in the number of embryos at both cleavage and blastocyst stage between two treatment groups (4.3 for Gonal-f® cohort vs. 3.5 for biosimilar cohort). In group A (<35 years of age), cleavage-stage transfers were carried out in more number of patients in the biosimilar cohort (28%) than in patients of the Gonal-f® cohort (22%), whereas blastocyst-stage transfers were higher in the Gonal-f® cohort (73%) compared to biosimilar cohort (67%). In group B (≥35 years of age), the number of cleavage-stage and blastocyst-stage transfers were comparable in both Gonal-f® and biosimilar cohorts [Table 2]. Significantly higher proportion

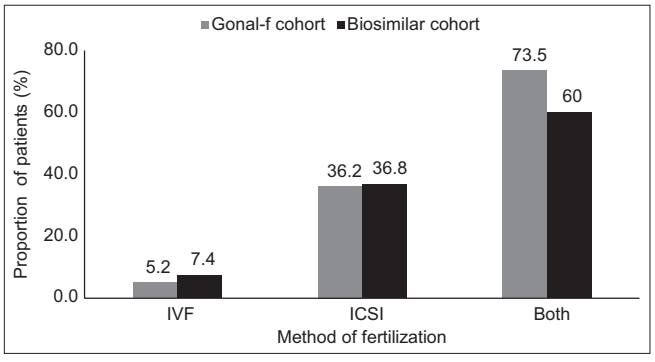

Figure 1: Distribution of patients undergoing ART based on method of fertilisation. ART: Assisted reproductive technology

Table 1: Demographic and baseline clinical characteristics of the study population

Parameters	Group A (<35 years)			Group B (≥35 years)		
	Gonal-f® (*n*=98)	r-hFSH biosimilar (*n*=136)	*P*	Gonal-f® (*n*=76)	r-hFSH biosimilar (*n*=54)	*P*
Age (years), mean±SD (95% CI)	30.3±2.1 (29.9–30.8)	29.2±3.3 (28.6–29.8)	0.0001*	37.5±2.4 (36.8–38.1)	36.7±2.3 (35.7–37.7)	0.288
Number of patients aged <35 years	98	136	-	-	-	-
Number of patients aged ≥35 years	-	-	-	76	54	-
AFC (*n*), mean±SD (95% CI)	13.9±5.9 (12.7–15.1)	13.6±5.7 (12.6–14.7)	0.535	11.4±4.8 (10.1–12.7)	12.8±7.7 (9.4–16.2)	0.381
AMH (ng/mL), mean±SD (95% CI)	4.3±4.7 (3.28–5.23)	5.4±3.5 (4.7–6.0)	0.048*	3.3±2.6 (2.6–4.0)	4.2±3.0 (2.9–5.5)	0.133
GN dose (IU), mean±SD (95% CI)	2806.3±733.3 (2653.6–2959.0)	2618.8±682.5 (2493.8–2743.8)	0.038*	3436.2±906.5 (3193.4–3678.9)	3171.6±879.7 (2781.6–3561.6)	0.735
Protocol (*n*), *n* (%) (95% CI)						
Agonist	37 (37.8) (0.3–0.5)	66 (48.5) (0.4–0.6)	-	21 (27.6) (0.2–0.4)	8 (14.8) (0.1–0.5)	
Antagonist	3 (3.1) (0–0.1)	1 (0.7) (0.0002–0.04)	-	3 (4.0) (0.01–0.1)	0	
Adjuvants (*n*), *n* (%) (95% CI)						
GH	13 (13.3) (0.1–0.2)	11 (8.1) (0.0–0.1)		26 (34.2) (0.3–0.5)	6 (10.7) (0.1–0.4)	
Letrozole	-	-		1 (1.3) (0.0–0.1)	0	
E2 priming	-	-		1	-	
Number of oocytes retrieved, mean±SD (95% CI)	13.3±6.1 (12.1–14.6)	14.4±6.0 (13.3–15.5)	0.184	11.5±5.0 (10.1–12.8)	13.2±7.7 (9.8–16.6)	0.266

*Significant difference between the two groups. AMH=Anti-mullerian hormone, CI=Confidence interval, *n*=Number of patients, r-hFSH=Human recombinant follicle stimulating hormone, BMI=Body mass index, AFC=Antral follicle count, E_2=Estradiol, hCG=Human chorionic gonadotropin, SD=Standard deviation, GN=Gonadotropin, GH=Growth hormone

Table 2: Subgroup analysis of reproductive outcomes

Parameters	Group A (<35 years)				Group B (≥35 years)			
	Gonal-f® (*n*=118)	r-hFSH biosimilar (*n*=166)	*P*	OR (95% CI)	Gonal-f® (*n*=118)	r-hFSH biosimilar (*n*=166)	*P*	OR (95% CI)
Number of embryos[$] on day 6, mean±SD (95% CI)	3.7±2.5 (3.15–4.19)	4.4±3.0 (3.8–4.9)	0.158		3.2±2.2 (2.6–3.8)	5.7±4.3 (3.8–7.6)	0.012*	
Embryo transfers								
Cleavage-stage transfers	26 (22)	46 (27.7)			11 (20)	05 (21.7)		
Blastocyst-stage transfers	86 (72.8)	111 (66.9)			40 (72.7)	17 (74)		
Double transfers	3 (2.5)	3 (1.8)			3 (5.4)	0		
No transfers/cancelled transfers	3 (2.5)	6 (3.6)			1 (1.8)	1 (4.3)		
Number of embryos transferred[$], mean±SD (95% CI)	3.0±2.8 (2.4–3.6)	2.0±0.6 (1.9–2.1)	0.001*		2.7±3.0 (1.9–3.5)	1.8±0.5 (1.6–2.0)	0.080	
Number of good quality embryos (cleavage/blastocyst)	5.1±2.9	4.8±3.1			4.6±3.3	6.1±4.3		
Number of patients, embryo[$] quality, *n* (%)								
Good	97 (82.2)	114 (68.7)			47 (85.4)	17 (73.9)		
Poor	21 (17.8)	50 (30.1)			8 (14.5)	6 (26.1)		
Clinical pregnancy rate (positive), *n* (%) (95% CI)	58 (59.2) (0.49–0.7)	54 (39.7) (0.3–0.5)	0.012*	2.2 (1.31–3.79)	35 (46.1) (0.4–0.6)	8 (14.8) (0.1–0.5)	0.046*	2.6 (1–6.75)
LBR (full term), *n* (%) (95% CI)	42 (43) (0.3–0.5)	24 (17.7) (0.1–0.3)	0.0001*	2.6 (0.41–16.83)	24 (31.6) (0.2–0.5)	5 (9.3) (0.1–0.4)	0.264	NA[#]
Miscarriage rate, *n* (%) (95% CI)	5 (9.8) (0.0–0.1)	10 (18.9) (0.0–0.1)	0.188	0.5 (0.15–1.48)	6 (7.9) (0.0–0.2)	0	0.187	NA[#]

*Significant difference between the two groups, [$]Embryos at cleavage/blastocyst stage, [#]The OR could not be calculated for miscarriage and LBR in case of Group B as in at least one case the value of the variable was zero. CI=Confidence interval, SD=Standard deviation, *n*=Number of patients, OR=Odds ratio, r-hFSH=Human recombinant follicle stimulating hormone, NA=Not available, LBR=Live birth rate

of patients of the Gonal-f® cohort had good quality embryos than patients of the biosimilar cohort (82.2% vs. 68.7%; $P = 0.002$), suggesting superior clinical efficacy of Gonal-f® to its biosimilars.

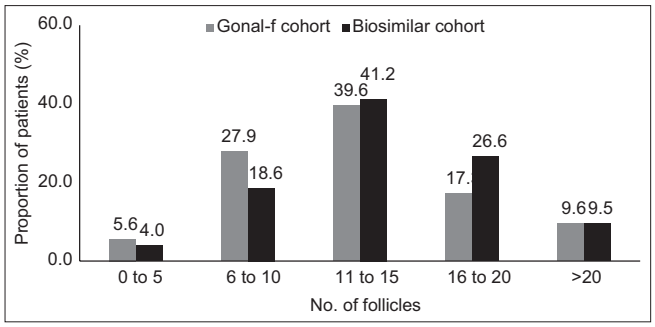

Figure 2: Distribution of patients based on number of follicles post ovarian stimulation

The distribution of the proportion of patients based on number of follicles was comparable in both Gonal-f® and biosimilar cohort [Figure 2]. The majority of the patients in both the cohorts had around 11–15 follicles on the day of trigger (Gonal-f®: 39.6%; biosimilar cohort: 41.2%). The number of patients with <10 follicles were comparatively higher in the Gonal-f® cohort than in the biosimilar cohort, whereas number of patients with 15, 20 or >20 follicles was higher in the biosimilar cohort [Figure 2]. It is noteworthy that although patients receiving Gonal-f® has less follicles, they still had better quality embryos compared to patients receiving biosimilars.

A comparison of reproductive outcomes between the two study groups has been given in Table 2. The rate of clinical pregnancy was higher in patients of the Gonal-f® cohort (59.2%) compared to patients of the biosimilar cohort (39.7%). Similarly, the full term LBRs were reported to be higher in the Gonal-f® cohort (43%) than the biosimilar cohort (17.7%), suggesting better reproductive outcomes with Gonal-f® as compared to its biosimilars [Table 2]. A higher likelihood of having a clinical pregnancy was observed with Gonal-F compared with biosimilars, both in the group A cohort (OR: 2.2, 95% CI: 1.3–3.8) and in the group B cohort (OR: 2.6, 95% CI: 1.0–6.8) [Table 2]. Similarly, patients who received Gonal-F had 2.6 times higher likelihood of a full-term birth compared to patients who received biosimilars (OR: 2.6, 95% CI: 0.4–16.8). Furthermore, there was a 53% lower chance of a miscarriage in patients who received Gonal-F than its biosimilars (OR: 0.5, 95% CI: 0.1–1.5) [Table 2]. However, both the differences were not statistically significant.

No major side effects were observed in the patients in any of the cohorts, other than pain and local allergic reaction in few cases.

Discussion

Human FSH is one of the critical drugs in ART over the last decades. r-hFSH, developed using recombinant DNA technology, is now widely employed to induce ovulation in patients undergoing controlled ovarian stimulation for ART.[7,8] Pre-clinical studies on animal models have demonstrated that r-hFSH formulations are safe and have no teratogenic, mutagenic or clastogenic effects. By the time of implantation, r-hFSH is undetected in blood samples and accidental exposure to this hormone in early stages of pregnancy has no detrimental effect on the foetus.[9-12] Among the r-hFSH preparations, Gonal-f® (follitropin alpha) is a commonly used r-hFSH fertility drug, which has been approved by the European Medicines Agency (EMA) in 1995[13] and United States Food and Drug Administration (US FDA) in 1997[14] for the induction of multifollicular development in women undergoing ART.[15]

However, follicle-stimulating hormone (FSH) treatment makes up a substantial proportion of the costs associated with ART,[16] and considering this aspect, biosimilars of r-hFSH have been introduced as part of clinical practice and are believed to be crucial for improving access to biological therapies for patients. The FDA defines a biosimilar as 'a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product'.[3] Currently, several licensed biosimilars for follitropin such as Ovaleap®, Bemfola®, Pergoveris®, Primapur®, Follitrope®, Elonva®, Rekovelle® and Clinnal-f® are being used across the world in clinical settings. Bemfola®, the first r-hFSH alpha biosimilar, was launched in Europe in 2014 and has been found to be similar in clinical benefit rates as Gonal-f® across all patient subpopulations as per findings of the real-world study of ART in France (REOLA) clinical trials. The REOLA trial also demonstrated that biosimilar r-hFSH can be as effective as the originator r-hFSH in a real-world setting.[17] Nevertheless, there is the need for comparative efficacy and safety data from real-world clinical practice to facilitate decision making on adoption and switch to biosimilar from originator molecule.

Our findings indicate higher effectiveness of Gonal-f® compared to biosimilars in terms of clinical pregnancy rate and LBR, with improved reproductive outcomes among women belonging to the older age group (≥35; group B) as well as in younger patients (<35 years; group A) who received Gonal-f® treatment. Patients receiving Gonal-f® had better quality embryos in spite of lower number of oocytes than patients receiving biosimilars. Likewise, better outcomes were seen with Gonal-f® treatment than with biosimilars treatment in terms of lower rates of miscarriage and preterm births. These findings are similar to those reported in a systematic review and meta-analysis by Chua *et al*., where better reproductive outcomes were achieved with Gonal-f® compared to its biosimilars.[15] Additionally,

a significant increase in good quality of embryos were observed at cleavage and blastocyst stage, which established a positive association of both pregnancy rates and LBR. Our findings suggest better embryological outcomes and reproductive outcomes among Gonal-f® as compared to its biosimilars. Analysis of cost-effectiveness of Gonal-f® compared to its biosimilars has not been done in this study. These findings will add to the evidence base and aid clinical decision making on the choice of FSH for ART.[18-20]

Clinical pregnancy rates are usually considered a good indicator of the efficacy of treatment. Our study reported superior clinical pregnancy rates in the Gonal-f® cohort (59.2% vs. 46.1%; group A vs. group B), which are comparatively higher than the rates reported in previous publications (between 23% and 39%).[21-23] However, in our study, patients treated with Gonal-f® yielded a higher clinical pregnancy rate as compared to those treated with biosimilars (39.7% vs. 14.8%; group A vs. group B). The higher clinical pregnancy could be due to the improved quality and higher quantity of oocytes. Findings of this study align with previously published literature which demonstrated a clinical pregnancy rate of 25% in the overall study sample and 34.5% in women with embryo transfer, when treated with Gonal-f®, higher than the clinical pregnancy rate among those treated with Ovaleap®.[24] Similarly, a retrospective study reported higher clinical pregnancy rate among the Gonal-f® cohort (35.6%) as compared to those treated with Ovaleap®, thereby suggesting Gonal-f® to yield higher clinical pregnancy rate compared to its biosimilar.[23] Additionally, our study findings were in contrast to certain studies which proved similar clinical pregnancy rates between biosimilars and originator.[25,26]

A detailed knowledge of the advantages and disadvantages of each gonadotropin preparation can aid in the prediction of the ovarian response and in increasing the LBR.[5] An increased LBR was reported in this study, among those treated by Gonal-f® compared to biosimilars belonging to both age groups (43% vs. 17.7%-group A; 31.6% vs. 9.3%-group B). Previous studies have also shown a similar trend.[15,18] An analysis of the French National Health System (SNDS) database showed that reference r-hFSH-alfa was associated with significantly higher cumulative LBR than highly purified menotropin or r-hFSH-alfa biosimilars among 214,539 stimulations.[27] However, findings of this study are in contrast to a previously published literature that reported no significant difference in LBR among those treated by originator or its biosimilar, suggestive of equivalent clinical efficacy.[21,28] According to Mastrangeli *et al*., differences in the LBR can be explained by differences in structural profiles and manufacturing processes in the biosimilar and reference products, thereby influencing FSH receptor activation and therefore biological activity.[29]

This study reports comparable values in terms of miscarriage rate among both the groups, which align with the findings of a previously published study that demonstrated similar results in terms of miscarriage rate, pregnancy rate and LBR with the use of corifollitropin-α versus daily r-hFSH.[9] Similarly, number of oocytes retrieved were also comparable. Albeit, higher percentage of good quality embryos were observed among women who were treated with Gonal-f® compared to biosimilars (82.2% vs. 68.7%-group A; 85.4% vs. 73.9%-group B). Moreover, slightly higher percentage was demonstrated among women of age group ≥35 years. The findings of various studies have suggested a biosimilar to be of less or equivalent effectiveness compared to its originator in terms of clinical factors and even cost.[15,17,30] Therefore, originator Gonal-f® continues to remain as the choice of medication, over its biosimilar, in ART.

In previous studies, LBR, the most important endpoint in IVF, has been considered as secondary outcome, thus limiting data in order to arrive at a meaningful conclusion on the equivalence of Gonal-f® to its biosimilars. LBR is a crucial outcome of ART, with an increasing consensus on correlation between ongoing pregnancy and LBR;[31] and having considered LBR as a primary outcome is the strength of this study. The analysis of other parameters such as clinical pregnancy rate, miscarriage rate, number of good embryos, number of embryos transferred, among a larger sample size with multiple biosimilars adds to the strength of this study. Although, statistically adequate prospective randomised controlled trials (RCTs) provide robust evidence, thereby suggesting the necessity for RCTs. In addition, the cost-effectiveness, treatment complexity, patient burden and pregnancy complications of both products should be taken into account in future analyses.

Despite the positive relation between Gonal-f® and reproductive outcomes, certain limitations need to be considered in this study. The retrospective study design may obscure bias, preventing firm conclusions from being drawn. Other potential drawbacks could be the unequal sample size in both groups which could affect the success rate of outcomes.

In conclusion, the results of this study show that patients receiving Gonal-f® have better pregnancy rates and LBR than those receiving biosimilars in a real-world setting. Real-world studies comparing both FSH preparations should be carried out to aid clinicians and patients while choosing follitropin alpha in ART.

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Conflicts of interest

There are no conflicts of interest.

Data availability

The data that support the findings of the current study are available from the corresponding authors upon reasonable request.

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