

## Original Research Article

# A retrospective, observational, single center study of gonadotropin-releasing hormone agonist protocols at the Reproductive Center of Farah Hospital in Jordan

Zaid Kilani<sup>1</sup>, Mohammad Shaban<sup>2\*</sup>

<sup>1</sup>General Director, Farah Hospital, Amman, Jordan

<sup>2</sup>Department of Gynecology and Assisted Reproduction, Farah Hospital, Amman, Jordan

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### \*Correspondence:

Dr. Mohammad Shaban,

E-mail: [tshaban82@yahoo.com](mailto:tshaban82@yahoo.com)

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### ABSTRACT

**Background:** Data on infertility and in vitro fertilization (IVF) are incomplete and uncertain in Jordan and worldwide because of difficulties in evaluating infertility in the general population. This study aimed at comparing the effectiveness of the gonadotropin-releasing hormone agonists (GnRH-a) long and short protocols as part of IVF or intracytoplasmic sperm injection.

**Methods:** This observational, retrospective, comparative, longitudinal study was conducted in a reproductive center in Jordan. It reviewed data charts from women who took GnRH-a for IVF, from 2010 to 2013. These were categorized in Group A (long-term GnRH-a: single 3.75 mg-monthly injection) or Group B (short-term GnRH-a: multiple daily 0.1 mg injections). The primary endpoint was the rate of ongoing clinical pregnancy (number of pregnancies/number of women) and live birth rate in fresh cycle/protocols.

**Results:** Out of 1,946 eligible women, 471 underwent the long-term treatment of GnRH-a administration and 1,523 the short-term treatment. The women's mean age was  $29.61 \pm 3.80$  years old. Out of the 471 women in Group A, 216 (45.9%) women had ongoing clinical pregnancy, of whom 69 (31.9%) had live births. In the short-protocol group, 485 (31.8%) women had ongoing clinical pregnancy, of whom 133 (27.4%) had live births.

**Conclusions:** GnRH-a long protocol is more effective than the short protocol regardless of the agonist formulation used in subfertile women/men who underwent IVF/ intracytoplasmic sperm injection.

**Keywords:** Fertility, GnRH-agonists, Implantation, Infertility, In vitro fertilization

## INTRODUCTION

According to the World Health Organization, infertility is defined as “a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse” (WHO-ICMART glossary).<sup>1</sup> It is characterized by the inability or difficulty for a man, a woman or a couple to carry a pregnancy to term, i.e. resulting in a live birth.<sup>2</sup> In total, 80% of couples achieve

a pregnancy within the first six cycles of fertility-focused intercourse. Otherwise, hypofertility must be suspected and 55% of couples suffering from the latter may have a pregnancy within 36 months of regular unprotected sexual intercourse.<sup>3</sup> If no pregnancy is achieved despite 48 months of regular sexual relations without using contraception, 5% of the couples are known to be infertile with a merely no chance of pregnancy.<sup>4</sup> The World Health Organization estimates that 80 million people worldwide suffer from infertility<sup>5</sup> and approximately 10%

of couples seeking a live birth are infertile.<sup>6</sup> In addition to the diagnosis and the etiology assessment of infertility, reproductive medicine involves a large number of medical activities, including the treatment of infertility, and the study of infertility from the epidemiological point of view. From one side, the gonadotropin-releasing hormone agonists (GnRH-a) were introduced into in vitro fertilization (IVF) superovulation regimens in the late 1980s and have become established as a component of standard regimens in most centers worldwide.<sup>7</sup>

GnRH-a are used for better control of ovarian hyperstimulation during the administration of exogenous follicle-stimulating hormone (FSH). Typically, after GnRH-a have induced a state of hypoestrogenism, exogenous FSH is given to stimulate ovarian follicle, followed by human chorionic gonadotropins (hCG) to trigger oocyte release. Each style of GnRH-a regimen (long, short or ultrashort) is associated with particular advantages and disadvantages. In general the "long-protocol" approach tends to be the most widely used.<sup>8</sup>

Furthermore, treatment modalities for infertility by IVF and GnRH-a include women with polycystic ovarian syndrome (PCOS).<sup>9</sup> The long GnRH-a protocol has been widely used in the treatment cycles of assisted reproductive technology and in women with PCOS to significantly reduce pregnancy loss and improve the cumulative pregnancy rate.<sup>10,11</sup>

On the other side, data on infertility and IVF in Jordan, as elsewhere in the world, are incomplete and uncertain. This is due to difficulties in evaluating infertility in the general population. In fact, very few studies on the epidemiological profile of infertility as well as the effectiveness of treatments with GnRH-a for IVF and intracytoplasmic sperm injection (ICSI) were conducted in Jordan. Since it was established in Jordan, the reproductive center of Farah Hospital has been responsible for the management of infertility.

Therefore, this observational study aimed primarily at comparing the effectiveness of long-term GnRH-a treatment to short-term treatment in a retrospective manner, in women who have undergone IVF/ICSI.

The secondary objectives of this study were to assess the effectiveness of GnRH-a in sub-groups of women with PCOS, of different age groups and poor responders, and to determine the correlation between the number of embryos transferred and the age of the mother at procedure and the number of previous cycles.

## **METHODS**

### ***Study design***

This was a single center, observational, retrospective, comparative, longitudinal study conducted at the reproductive center of Farah Hospital in Jordan. The

study did not involve any change in the clinical management of women and required no specific consultation.

### ***Study population***

This study was conducted in women who took GnRH-a for IVF, from 2010 to 2013. Women were compared between two groups: Group A (long-term treatment of GnRH-a administration: single monthly injection of 3.75 mg), Group B (short-term treatment of GnRH-a administration: multiple daily injections of 0.1 mg).

### ***Inclusion criteria***

- Sub-fertile women/men who had undergone IVF/ICSI with indications for IVF/ICSI (tubal factor, PCOS, poor responder, male factor or unexplained factor IVF)
- Women who undertook standardized GnRH-a, long or short protocols
- Women whom basal FSH levels were  $\leq 10$  IU/L, and aged  $\leq 35$  years at the time of enrolment.

Subfertility was defined as any form of reduced fertility with prolonged time of unwanted non-conception. The persons were not eligible in case of endometriosis, adenomyosis, IVF performed for sex selection, or non-availability of any assessable medical records. PCOS was not an exclusion criterion.

### ***Data collected***

Data were retrospectively retrieved from the women's medical records and reported on Excel sheets available at Farah Hospital by a study technician. No Case Report Form was needed. The following information were collected: baseline characteristics (year of birth of the woman, basal FSH, type of IVF protocol: long/short, and country of residence), data collected at cycles of treatment (number of cycles till pregnancy, type and duration of infertility, days of gonadotropin stimulation, form and total dose of GnRH-a per cycle, and day of administration of the GnRH-a and dose used per protocol), hormone profile on day 2 or 3 of the cycle (serum FSH, luteinizing hormone, estradiol and progesterone), ovarian stimulation characteristics (number of oocytes retrieved, injected and fertilized, fertilization rate, number of embryos transferred at day 3 or 5, number of follicles  $>15$  mm on hCG day, endometrial thickness on hCG day, implantation, clinical pregnancy, miscarriage and live birth).

Fertilization rate was computed as the proportion of oocytes fertilized compared to the number of oocytes injected. Clinical pregnancy was defined as a positive serum hCG result, with ultrasound evidence of a gestational sac and fetal heartbeat. Miscarriage was defined in women with an initially positive pregnancy test and ultrasound evidence of a gestational sac with a

fetal pole where pregnancy failed to develop by 12 weeks of gestation. Live birth was defined as pregnancies over 28 weeks per treatment cycle of ET. As for safety data, any physician facing an adverse event that may be due to a drug had to declare it to his regional pharmacovigilance center according to national and local applicable laws. This had to be done retrospectively before the study initiation.

### **Study endpoints**

The primary endpoint was the rate of ongoing clinical pregnancy (number of pregnancies/number of women) and live birth rate in fresh cycle per protocols. Secondary endpoints were the rate of implantation, cumulative ongoing pregnancy rate per woman, rate of miscarriage, cumulative birth rate per woman, number of oocytes retrieved, hormone profiles, rate of women with PCOS, number of cycles required for pregnancy, and correlation between the number of embryos transferred and the age of the mother at procedure and the number of previous cycles.

### **Statistical analysis**

To detect a difference as low as 5% in clinical pregnancy (for example, 11% vs 16% as in Youssef et al, and in live birth rates between the short and long protocols with 90% power and a 5% significance level using the chi-squared test, 2,000 women were to be included retrospectively in the study.<sup>12</sup> Continuous data were given as mean±standard deviations, medians and quartiles (Q1 and Q3), and categorical variables were expressed as numbers and percentage. Data were analyzed for all eligible women who were consulted at Farah Hospital and for whom data were collected for evaluation for a 4-year period from January 2010 until December 2013. Some endpoints were compared between the long and short protocols using the independent t-test or Wilcoxon ranks sum test for numeric variables or the chi-squared test or Fisher's exact test for categorical variables.

The correlation between the number of embryos transferred and the age of mother during the attempt and the number of previous cycles was determined using a multiple logistic regression, with the ongoing clinical pregnancy being the dependent variable and independent variables being predictors of the clinical pregnancy such as the age of the mother, the country of residence, the IVF protocol (short vs. long), type of infertility, duration of infertility and the hormonal profile. Statistical analyses were performed using IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA). Statistical tests are two-sided at the 5% statistically significance threshold.

### **Ethical considerations**

This study was approved by the Institutional Review Board (IRB) of Farah Hospital on 23 January 2016, and an informed consent waiver was sought by the IRB given

the retrospective study design. It was conducted in compliance with the study protocol, the applicable regulatory requirements in Jordan, and the Good Pharmacoepidemiology Practices (GPP).

A unique identifier was assigned by the investigator to each participant to protect their identity and used in lieu of their name to ensure confidentiality

## **RESULTS**

In total, 1,946 women were included in the database of whom 471 underwent the long-term treatment of GnRH-a administration and 1,523 the short-term treatment with GnRH-a. Two couples were excluded for having an IVF performed for sex selection. Therefore, statistical analysis was performed over 1,944 eligible couples.

### *Demographic characteristics of the women*

The mean age of the women undergoing IVF at Farah Hospital was 29.61±3.80 years old, it was 28.76±3.84 years old in Group A and 29.88±3.75 years old in Group B. Most of the women (n=699; 35.1%) underwent IVF in 2010. Also, most of the women (n=532; 26.7%) were resident in Jordan followed by Iraq (n=341, 17.1%), and Libya (n=256, 12.8%) (Table 1).

### **Primary endpoint**

Out of the 471 women in Group A, 216 (45.9%) women had ongoing clinical pregnancy, of whom 69 (31.9%) had live births. In the short-protocol group, 485 (31.8%) women had ongoing clinical pregnancy, of whom 133 (27.4%) had live births (Table 2).

### **Secondary endpoints**

#### *Clinical characteristics of the couples*

In the study population, the 1,994 couples were reported to have infertility for an average period of 5.38±3.74 years before undergoing IVF. The mean duration of infertility in the long-protocol group was 4.59±3.35 years and seemed to be lower compared to the short-protocol group (5.63±3.82 years).

The major cases of infertility were man-related: 336 (71.3%) cases in Group A vs. 1,057 (69.5%) in Group B (Table 3). Regarding the hormone profile of women undergoing IVF on day 2 or 3 of the cycle, the mean serum FSH was 4.72±1.93 IU/mL amongst the 1,994 women. It was 2.61±1.32 IU/mL in Group A vs. 5.37±1.58 IU/mL in Group B.

In Group A, 61.6% of the 286 women received multiple daily injections of 0.1 mg of GnRH-a per cycle vs. 99.9% (n=1,520) in the short-protocol group (p <0.001). The remaining women in each group received a single monthly injection of 3.75 mg of GnRH-a per cycle. Also,

the mean number of follicles >15 mm on hCG day tends to be higher in Group A (7.49±2.13) compared to Group

B (6.91±2.07) (Table 3).

**Table 1: Demographic characteristics compared between the two protocols.**

Variable	Overall (N=1,994)	Group A (n=471)	Group B (n=1,523)
Age (mean±SD)*	29.61±3.80	28.76±3.84	29.88±3.75
Year	2010	238 (50.5%)	461 (30.3%)
	2011	109 (23.1%)	446 (29.3%)
	2012	85 (18.0%)	451 (29.6%)
	2013	39 (8.2%)	165 (10.8%)
Country	Jordan	238 (50.5%)	294 (19.3%)
	Iraq	48 (10.2%)	293 (19.2%)
	Libya	30 (6.4%)	225 (14.8%)
	KSA	23 (4.9%)	204 (13.4%)
	Oman	23 (4.9%)	123 (8.1%)
	UAE	24 (5.1%)	76 (5.0%)
	Palestine	17 (3.6%)	63 (4.1%)
	Kuwait	16 (3.4%)	53 (3.5%)
	Yemen	8 (1.7%)	59 (3.9%)
	Syria	12 (2.5%)	35 (2.3%)
	Qatar	10 (2.1%)	28 (1.8%)
	America	6 (1.3%)	28 (1.8%)
	Other countries	16 (3.4%)	42 (2.8%)

Abbreviations: max: maximum; min: minimum; SD: standard deviation. KSA: Kingdom of Saudi Arabia.

**Table 2: Pregnancy per age group and per number of embryos transferred and then stratified by protocol.**

Variable	Pregnancy	p-value	Pregnancy in Group A (n=471)	p-value	Pregnancy in Group B (n=1,523)	p-value
<b>Age categories (years)</b>						
17-25	96/294 (32.7%)	0.330	40/97 (41.2%)	0.305	56/197 (28.4%)	0.270
>25-35	605/1,700 (35.6%)		176/374 (47.1%)		429/1326 (32.4%)	
<b>Number of embryos transferred</b>						
1	28/190 (14.7%)	<0.001*	4/32 (12.5%)	0.001*	24/158 (15.2%)	
2	161/436 (36.9%)		61/113 (54.0%)		100/323 (31.0%)	
3	375/939 (39.9%)		115/242 (47.5%)		260/697 (37.3%)	
4	106/247 (42.9%)		26/52 (50.0%)		80/195 (41.0%)	
5	12/18 (42.9%)		5/9 (55.6%)		7/19 (36.8%)	

\*Significant difference between the short and long protocols: two-sided significance level at 5%, Data were analyzed using the chi-squared test or Fisher's exact test for categorical variables.

**Pregnancy outcomes of the treatment groups**

Following ovarian stimulation with GnRH-a, the mean number of oocytes retrieved was 11.11±5.51 in Group A vs. 9.20±4.91 oocytes in Group B (p <0.001).

Moreover, the fertilization rate was non-significantly higher in Group A (64.57±25.98%) compared to group B (62.32± 26.88%). 242 (54.6%) women in Group A were transferred three embryos vs. 697 (50.1%) in group B (p=0.044) (Table 4).

As for the implantation rate, it was 57.6%±17.8% (median: 50%, Q1: 50%; Q3: 50%) in 379 analyzable women undergoing any of the IVF protocols. Also, 84.2% of the 379 women had an implantation rate of 50% and 14.8% had implantation rate of 100%.

The rate of m Abbreviation: 95% CI: 95% confidence interval. aData compared using independent t-test or Wilcoxon ranks sum test for numeric variables. Data compared using the chi-squared test or Fisher's exact test for categorical variables is carriage was 29.64% in 360 analyzable women.

**Table 3: Women characteristics compared between the two treatment protocols.**

Variable	Overall (N=1,994)	Group A (n=471)	Group B (n=1,523)
Duration of infertility (year) <sup>a</sup>	5.38±3.74	4.59±3.35	5.63±3.82
Type of infertility <sup>b</sup>			
Missing data	266 (13.4%)	60 (12.7%)	206 (13.5%)
Male	1,393 (69.9%)	336 (71.3%)	1,057 (69.5%)
Female	200 (10.0%)	45 (9.6%)	155 (10.2%)
Both	105 (5.3%)	21 (4.5%)	84 (5.5%)
Unknown	28 (1.4%)	9 (1.9%)	19 (1.2%)
FSH (IU/mL) <sup>a</sup>	4.72±1.93	2.61±1.32	5.37±1.58
PRL (IU/mL) <sup>a</sup>	17.03±11.25	16.16±9.65	17.28±11.65
LH (IU/mL) <sup>a</sup>	3.60±2.23	2.03±1.99	4.09±2.07
E2 (IU/mL) <sup>a</sup>	30.29±19.16	18.44±17.17	33.93±18.25
P4 (IU/mL) <sup>a</sup>	1.06±1.11	0.85±1.11	1.13±1.10
TSH (IU/mL) <sup>a</sup>	2.20±1.67	2.09±1.20	2.23±1.78
No. of follicles on the day of hCG for final follicular maturation <sup>a</sup>	7.04±2.095	7.49±2.13	6.91±2.07
Formulation used [total dose of GnRH-a/cycle (mg)] <sup>b</sup>			
Multiple daily injection (0.1 mg)	1,806 (90.9%)	286 (61.6%)	1,520 (99.9%)
Single monthly injection (3.75 mg)	180 (9.1%)	178 (38.4%)	2 (0.1%)
HMG amount (IU) <sup>a</sup>	26.96±11.95	27.89±11.51	26.68±12.07
HMG duration (days) <sup>a</sup>	8.75±2.77	10.07±4.12	8.35±2.02
E2 (day of hCG) (IU/mL) <sup>a</sup>	1,214.48±943.13	1,055.99±778.54	1,263.51±983.58
P4 (day of hCG) (IU/mL) <sup>a</sup>	1.33±0.93	1.06±0.68	1.41±0.98

E2: estradiol, FSH: follicle-stimulating hormone, hCG: human chorionic gonadotropins, HMG: human menopausal gonadotropin, LH: luteinizing hormone, Max: maximum; Min: minimum, P4: progesterone, PRL: prolactin, SD: standard deviation, TSH: thyroid stimulating hormone, <sup>a</sup>Data compared using independent t-test or Wilcoxon ranks sum test for numeric variables, <sup>b</sup>Data compared using the chi-squared test or Fisher's exact test for categorical variables.

**Table 4: Comparison of outcomes between the two treatment groups.**

Variable	Group A (n=471)	Group B (n=1,523)
Number of oocytes retrieved <sup>a</sup>	11.11±5.51	9.20±4.91
Number of oocytes injected <sup>a</sup>	8.54±4.52	7.32±3.95
Number of oocytes fertilized <sup>a</sup>	5.44±3.46	4.53±3.04
Fertilization rate <sup>a</sup>	64.57±25.98	62.32±26.88
Number of embryos transferred	2.76±0.82	2.71±0.89
1 <sup>b</sup>	32 (7.1%)	158 (11.4%)
2 <sup>b</sup>	113 (25.2%)	323 (23.2%)
3 <sup>b</sup>	242 (54.0%)	697 (50.1%)
4 <sup>b</sup>	52 (11.6%)	195 (14.0%)
5 <sup>b</sup>	9 (2.0%)	19 (1.4%)
Clinical pregnancy <sup>b</sup>	Yes	216 (45.9%)
	No	255 (54.1%)
	95% CI	(41.4%-51.4%)
Live births amongst those with clinical pregnancy <sup>b</sup>	Yes	69 (31.9%)
	No	147 (68.1%)
	95% CI	(25.7%-38.2%)

**Predictors of pregnancy**

FSH was excluded from the final model because of its huge collinearity with IVF protocol, people with high levels of FSH were put on short protocol while those with

low levels of FSH were put on long protocol. Also, while data were missing for the duration of infertility; it was maintained in the final model since it is still considered an important predictor for pregnancy (Table 5). In parallel, if the duration of infertility and FSH were

excluded from the model, the latter will be a bit different where IVF protocol type will remain significant, the age of the mother and the number of follicles will become

non-significant and living in Jordan becomes significant whereby women living in Jordan have better chances of pregnancy than those outside the country.

**Table 5: Predictors of pregnancy.**

Variable	OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
<b>IVF protocol</b>				
Short	1	<0.001*	1	0.016*
Long	1.813 (1.468-2.238)		1.456 (1.071-1.978)	
Age of mother (years)	1.009 (0.985-1.034)	0.454	1.039 (1.008-1.071)	0.012*
<b>Country</b>				
Others	1	<0.001*	1	0.412
Jordan	1.502 (1.225-1.841)		1.113 (0.857-1.446)	
<b>Type of infertility</b>				
Male	1	0.622	1	0.423
Female	0.818 (0.594-1.125)	0.216	0.762 (0.515-1.126)	0.173
Both	0.990 (0.654-1.500)	0.963	1.232 (0.745-2.037)	0.416
Unknown/missing	1.041 (0.802-1.353)	0.762	0.945 (0.688-1.297)	0.725
Duration of infertility†	0.944 (0.917-0.973)	<0.001*	0.937 (0.907-0.969)	<0.001*
LH	0.971 (0.930-1.013)	0.177	1.008 (0.954-1.066)	0.767
E2	0.993 (0.987-0.999)	0.018*	0.998 (0.991-1.005)	0.619
P4	0.948 (0.866-1.038)	0.249	1.001 (0.904-1.108)	0.987
Number of follicles on the day of hCG for final follicular maturation	1.057 (1.011-1.106)	0.014*	1.066 (1.011-1.124)	0.017*

\*Significant predictors: two-sided significance level at 5% using a multiple logistic regression, †N=424 missing duration of infertility.

Abbreviations: 95% CI: 95% confidence interval; E2: estradiol; hCG: human chorionic gonadotropins; IVF: in vitro fertilization; LH: luteinizing hormone; P4: progesterone; OR: odds ratio.

### **Sub-groups of women with polycystic ovarian syndrome**

The study was not able to address the first secondary objectives “to assess the effectiveness of GnRH-a in sub-groups of women with polycystic ovarian syndrome, of different age groups and poor responders” as 41 (3.98%) out of 1,030 women had PCOS (data were missing or not described in 964 women for PCOS variable).

### **DISCUSSION**

This retrospective study aimed to compare the effectiveness of GnRH-a long and short protocols as part of IVF or ICSI. It also aimed to assess the effectiveness of GnRH-a in sub-groups of women with PCOS, of different age groups and poor responders, and to determine the correlation between the number of embryos transferred and the age of the mother at procedure and the number of previous cycles. Although this study was conducted at Farah Hospital only, it would provide information that can be generalized to the regional level in Jordan about GnRH-a protocols as part of IVF treatment. The study collected and analyzed retrospective

data from 1,994 eligible women of whom 532 (26.7%) lived in Jordan. A total of 471 (23.6%) women underwent the GnRH-a long protocol vs. 1,523 (76.4%) women who underwent the GnRH-a short protocol. The long protocol consisted of a single monthly injection of 3.75 mg while multiple daily injections of 0.1 mg were performed in the short protocol. On a side note, 0.1 mg daily formulation is often used at Farah Hospital even in the long-agonist group i.e. daily injections of GnRH-a for one month. Also, the difference in formulation of GnRH-a between single and multiple injection for the long protocol was documented in the database. The analysis showed that around 60% of the women on the long protocol received multiple injections. Nonetheless, the ultimate goal of the present study is to compare the IVF outcomes according only to the GnRH-a long vs. short protocols regardless of the agonist formulation used. The study showed that the rate of clinical pregnancy was significantly higher in women undergoing the long protocol (45.9%) compared to the short protocol (31.8%) ( $p < 0.001$ ). Our results are consistent with the findings of a retrospective analysis of 531 women aged  $\geq 40$  years and who underwent cycles of intracytoplasmic sperm injection in Egypt whereby

pregnancy rate was significantly higher in the long protocol vs. short protocol.<sup>12</sup> Indeed, the long protocol achieved a pregnancy rate of 26.6% vs. 10.2% with the short protocol ( $p < 0.001$ ).<sup>12</sup> Another retrospective study conducted in China among 5,662 women of various age ranges showed that the clinical pregnancy rates of the four age categories (<31 years, 31-35 years, 36-40 years, and >40 years) were significantly higher than those in the short-protocol group.<sup>13</sup> On a similar note, the effectiveness of long protocol was demonstrated to outweigh the short protocol in IVF on the basis of clinical pregnancy rate per cycle started.<sup>14</sup>

Similarly, the rate of live births was significantly higher in women undergoing the long protocol (31.9%) compared to the short protocol (27.4%) ( $p < 0.001$ ). The other secondary outcomes such as the number of oocytes retrieved, number of oocytes injected, number of oocytes fertilized were significantly higher in women undergoing the long protocol compared to the short-protocol treatment, as supported by literature.<sup>12,13</sup> Nonetheless, the present study has few limitations. The first limitation is the retrospective collection of data from hospital data sheets. Most of the women ( $n=1,523$ , 76.4%) underwent the GnRH-a short protocol since most of them are non-Jordanian living outside Jordan. The women used to come on the beginning of the menstrual cycle and treatment has to be initiated to save time and costs of stay in Jordan. Thus, treatment protocols has to be tailored to the couples' circumstances, and which is contrary to specific protocols to be followed in the prospective studies. The second limitation is deficiency of data down the road of follow-up. After embryo transfer, most women stay for few days in Amman, Jordan then they start to leave the country, and follow-up communication will start to be lost due to many factors such as the educational and cultural backgrounds of the couples in addition to difficulties in some specific countries. Loss of woman follow-up led to a lower than expected results in terms of pregnancies, number of fetuses, number of miscarriages, number of live births and incidence of pregnancy anomalies. Data were only available in 379 women where the implantation rate was 57.6%. Our data were collected after continuous and manifold attempts to communicate with the couples. It is noteworthy to note that the follow-up system at Farah Hospital consists of recording the phone numbers of the husband and wife in addition to their email addresses (if available), and to instruct them to send the hospital any information regarding the pregnancy outcomes. If the couples fail to send the information, the hospital keeps trying to communicate with them through phone calls and emails. In conclusion, this study showed that the GnRH-a long protocol is more effective than the short protocol regardless of the agonist formulation used in subfertile women/men who had undergone IVF/ICSI with indications for IVF/ICSI (tubal factor, PCOS, poor responder, male factor or unexplained factor IVF) and who have basal FSH levels  $\leq 10$  IU/L and aged  $\leq 35$  years at the time of treatment initiation.

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