Follicular sensitivity index (FSI): a novel tool to predict clinical pregnancy rate in IVF/ICSI cycles

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Abstract

Purpose This study aims to introduce a new tool (the Follicular Sensitivity Index; FSI) for objective assessment of follicular responsiveness to exogenous gonadotropins and to evaluate its ability to predict the clinical pregnancy rate in women with unexplained infertility or tubal factor undergoing IVF/ICSI.

Methods FSI was calculated as preovulatory follicle count (PFC) $\times$ 100,000/[antral follicle count (AFC) $\times$ total received FSH doses]. One thousand women were included and were divided according to the FSI tertile values into three groups. The primary outcome was clinical pregnancy defined by the presence of an intrauterine gestational sac 5 weeks after embryo transfer.

Results There was progressive increase in the clinical pregnancy rate from the low to the high FSI groups (0.27 ± 0.4 vs 0.4 ± 0.4 and 0.58 ± 0.4 ; $p < 0.001$). Receiver operator curves showed that FSI had a greater area under the curve than those of the AFC, PFC, and the FSH dose (0.638 vs 0.509, 0.538, and 0.589 respectively). Multivariate logistic regression analysis showed that the correlation between FSI and pregnancy was independent of potential confounding factors like age and body mass index ($p < 0.001$).

Conclusion FSI can predict the clinical pregnancy rate in women with unexplained infertility or tubal factor undergoing IVF/ICSI using GnRH agonist protocol. Higher FSI values had significantly higher oocyte yield and fertilization and clinical pregnancy rates. Wider implications of these findings include the potential use of FSI to define absolute criteria of poor/good ovarian response in IVF/ICSI cycles, guide future IVF cycle management for the same couples, and guide cycle cancellation criteria for poor ovarian response.

Keywords Follicular sensitivity index · Unexplained infertility · IVF · ICSI · Ovarian response

Introduction

In vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) involve several steps, the first of which is controlled ovarian hyperstimulation (COH) [1]. Ovarian stimulation usually requires the careful administration of exogenous gonadotropins aiming to produce adequate number of oocytes without increasing the risk of ovarian hyperstimulation syndrome [2]. In COH, women respond differently to similar doses of exogenous gonadotropins. Different methods have been proposed to predict such responses [3, 4]. The mechanisms affecting the response of antral follicles to gonadotropins are not yet clear; however, it has been suggested that adequate response of antral follicles could be attributed to the presence of healthy granulosa cells [5]. Antral follicles that respond adequately to gonadotropins will most probably result in more favorable outcomes with higher chances of achieving pregnancy following IVF/ICSI [6].

Different methods have been proposed to objectively predict the follicular response to exogenous gonadotropins including follicular output rate (FORT) and ovarian sensitivity

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index (OSI) [7, 8]. The former represents the ratio of preovulatory follicle count (PFC) to the antral follicle count (AFC) while the latter represents the number of retrieved oocytes divided by the total FSH dose given for COH. Although FORT and OSI may reflect ovarian response to stimulation, they actually have two different concepts. FORT assesses the visible part of the ovarian reserve (number of follicles before and after stimulation) irrespective of the used FSH doses, while OSI is a measure of the ovarian function in which the overall ovarian response and the used FSH doses are considered irrespective of the AFC.

Genro et al. were the first to suggest using the FORT [7]. In their study, they evaluated the correlation between the clinical pregnancy and FORT in IVF cycles. They noted that clinical pregnancy rate increased progressively from the low to the high FORT groups [6]. Similar observation was also noted by Zhang et al. in women without polycystic ovarian syndrome (PCOS) [9] and more recently by Hassan et al. in women with unexplained infertility [10].

On the other hand, OSI was found to be correlated with anti-Müllerian hormone (AMH) [8] and was a better predictor of ovarian response to COH than the number of retrieved oocytes during IVF [11]. Huber et al. used OSI to define poor, normal, and high ovarian response to IVF in long gonadotrophin-releasing hormone (GnRH) agonist protocol [12].

It has to be noted that FORT does not consider the degree of ovarian stimulation during COH, and OSI does not consider AFC; furthermore, OSI cannot be calculated before ovum pickup, making it not suitable to guide the decision of ovum pickup in women with poor ovarian response. In an attempt to evaluate accurately the follicular responsiveness to exogenous FSH taking into account the degree of ovarian stimulation during COH and potentially being able to guide the decision of ovum pickup in women with POR, we are introducing the follicular sensitivity index (FSI) which is calculated using the formula ($FSI = PFC * 10,000 / AFC * \text{Total dose of FSH}$).

This study aims to introduce FSI as a new tool and to evaluate its ability to predict clinical pregnancy in women having potentially normal ovarian response, undergoing IVF/ICSI. Up to the best of our knowledge, this is the first study to introduce FSI as a new tool and to investigate the role of FSI and pregnancy rates in couples undergoing IVF/ICSI.

Methods

This was a prospective observational study done at a private fertility center (Dar Al-Teb fertility center, Giza, Egypt) in the period from May 2014 to October 2016. Approximately, 15,000 subfertile couples are treated at this center each year. The study was approved by the research ethics committee of Cairo University.

Inclusion criteria were couples with at least 2 years of unexplained infertility or those with tubal factor infertility; women's age from 20 to 42 years; and having both ovaries and with serum level of follicle stimulating hormone (FSH) and estradiol (E2) done on the second day of menstrual cycle less than 12 mIU/L and less than 50 pg/ml, respectively. All couples provided their informed written consent.

Diagnosis of unexplained infertility was based on the presence of normal semen analysis as defined by the WHO criteria [13], normal hysterosalpingography, and evidence of ovulation (mid-luteal serum progesterone exceeding 5 ng/ml) [14]. Tubal factor of infertility was diagnosed if hysterosalpingography or laparoscopy showed evidence of bilateral tubal obstruction.

Exclusion criteria were cases with endometriosis, abnormalities of the uterine cavity, uncontrolled diabetes, evidence of hydrosalpinx, allergy to gonadotropins, and women with expected poor ovarian response (POR) according to the Bologna criteria [15].

We canceled the cycles when the use of doses reaching 450 IU for 12 days has yielded only two follicles or less (16–22 mm in diameter). Also, in order to avoid the risk of ovarian hyperstimulation syndrome, we canceled the cycles if the ovarian stimulation has yielded 20 follicles or more with the leading 3 follicles ≥ 15 mm and serum E2 > 1600. Cases in which endometriosis was suspected were offered laparoscopy, and those with confirmed endometriosis were excluded.

Downregulation was achieved using Triptorelin (0.1 mg; Decapeptyl®, Ferring Pharmaceuticals, St-Prex, Switzerland) which was started in the mid-luteal phase of the preceding cycle. On the second day of menstrual cycle, we assessed serum FSH, luteinizing hormone (LH), prolactin, and E2 as well as the AFC which is the number of follicles measuring 3–10 mm using transvaginal ultrasound scan (Logiq C3 premium, GE, UK).

Ovarian stimulation using FSH (Fostimon®, Lugano, IBSA, Switzerland) was started on the second day of menstrual cycle. The starting dose of FSH was individualized according to the women's age and BMI [16] and ranged between 150 and 300 IU/day. The initial dose was then modified according to the patient's response. When ovarian stimulation has yielded at least 3 follicles, 16–22 mm in diameter, and E2 levels of 200 pg/ml per follicle, 10,000 IU of hCG (Choriomon®, IBSA) was administered. PFC (defined as the number of follicles measuring 16–22 mm in diameter) was assessed on the day of hCG administration using transvaginal ultrasound scan (Logiq C3, GE, UK). The FSI was calculated using the formula: $FSI = PFC * 10,000 / (AFC * \text{Total dose of FSH})$.

Oocytes were retrieved 34–36 h after hCG administration using transvaginal ultrasound. Fertilization of the retrieved oocytes was achieved by ICSI for Metaphase 2 (M2) oocytes and by IVF for other oocytes. Fertilization was confirmed

after 16–18 h by the presence of 2 pronuclei within the zygotes which were transferred to global culture medium (LifeGlobal, Ontario, Canada). Excellent quality embryos were defined as those containing 6–8 even blastomeres with <10% fragmentation at day 3.

Embryos were transferred on day 5. If possible, two embryos were transferred and the remaining embryos were cryopreserved. Progesterone vaginal suppositories (Prontogest® IBSA) 400 mg/day were used for luteal support. Serum β hCG measurement was performed 2 weeks after embryo transfer.

Sample size calculation

If we assumed that the least difference expected in the clinical pregnancy between the high and medium FSI groups would be 12% (55 and 43% respectively), the sample size needed should be 271 cases for each group with a total of 813 cases. We decided to study 1000 cases to count for any missing data and losses to follow-up. Chi-square test was used to calculate the sample size; we adjusted the alpha error at 0.05 and the power at 80%. We used the PS Power and Sample Size Calculations software, version 3.0.11 for MS Windows (William D. Dupont and Walton D. Vanderbilt, USA).

Statistical analysis

Data were described as mean $\pm$ standard deviation ($\pm$ SD), frequencies, and percentages when appropriate. We used the analysis of variance (ANOVA) test to compare continuous variables of the FSI groups, and we used the student *t* test to compare continuous variables of the pregnant and non-pregnant groups. Chi-square (χ^2) test was performed for comparisons of categorical data. A *p* value <0.05 was considered significant. We performed multivariate logistic regression analysis to find the possible independent correlations between the tested variables and their contributions. Receiver operator characteristic (ROC) curves were used to compare different clinical pregnancy rate predictors. We used SPSS for IBM (IBM Corp., Armonk, NY, USA) to perform all statistical calculations.

Results

We approached 1124 couples, and of these, 32 were excluded, 92 refused to participate, and 37 women had canceled cycles (12 for poor ovarian response, 32 to avoid ovarian hyperstimulation syndrome, and two for failure of fertilization). We conducted intention-to-treat analysis and included all canceled cycles in the analysis, but they were considered to have no oocyte yield, fertilization, or pregnancy.

We studied 1000 women who were divided into three groups according to the FSI tertile values: low FSI (*n* = 329) with FSI values below the 33rd percentile and moderate FSI (*n* = 340) with FSI values from zero to 43.01. There were no significant differences in the baseline characteristics among the groups. However, the clinical pregnancy rate showed a progressive increase from the low to the high FSI groups. Also, other parameters were higher in the high FSI groups including the number of retrieved oocytes, fertilization rate, total number of embryos available for transfer, and number of excellent quality embryos (Table 1).

Women who achieved pregnancy had lower age and BMI. They had higher FSI, more retrieved oocytes, fertilized oocytes, total number of embryos, and number of excellent quality embryos (Table 2). ROC curves showed that FSI had a greater area under the curve than those of the AFC, PFC, total FSH dose, FORT, and OSI (Table 3 and Figs. 1 and 2),

Discussion

In this study, the clinical pregnancy rate showed a significant and progressive increase from the low to the high FSI groups. Likewise, PFC, fertilization rate, the number of fertilized oocytes, and the total number of embryos increased from the low to the high FSI groups. These results suggest that FSI can objectively predict the follicular response to exogenous FSH, which is an important indicator of oocyte function. Follicles of high quality are expected to be more responsive to FSH than those of low quality, thereby requiring less doses of FSH during COH and subsequently resulting in higher PFC, higher FSI, and higher number of retrieved oocytes with higher fertilization rate and consequently higher number of embryos available for transfer. In our study, the number of excellent quality embryos was significantly fewer in the low FSI group which may indicate that women in the low FSI group were having lower quality oocytes. Supporting this is the finding that poor quality gametes were less likely to result in high-quality embryos [17].

Huber et al. reported similar results using OSI. They retrospectively studied 7520 IVF cycles with different indications of infertility [11]. Similar results were also reported by Gallot et al., Zhang et al., and Hassan et al., using FORT [6, 9, 10]. The role of FORT was initially evaluated in 322 infertile women (in the study by Gallot et al.) and in 1503 infertile non-PCOS women as well as 140 infertile PCOS women undergoing IVF/ICSI (in the study by Zhang et al.). Both studies observed that the retrieved oocytes, the total number of embryos, the proportion of good quality embryos, and pregnancy rate increased progressively from the low to the high FORT groups. However, they observed that the fertilization rate was not significantly different among the FORT groups. This is in

Table 1 Baseline characteristics and COH data in the FSI groups

	Low FSI ^a (<i>n</i> = 329)	Moderate FSI (<i>n</i> = 340)	High FSI (<i>n</i> = 331)	<i>P</i> value
Age	32.9 ± 4.9	32.8 ± 4.6	32.2 ± 5	0.116
Gravidity	0.8 ± 0.7	0.9 ± 0.7	0.8 ± 0.7	0.507
Parity	0.3 ± 0.6	0.4 ± 0.6	0.4 ± 0.6	0.32
Body mass index (kg/m ²)	28.5 ± 3.3	28 ± 3.2	28 ± 3.4	0.07
Duration of subfertility (years)	5.5 ± 2.2	5.5 ± 2.2	5.2 ± 2.2	0.131
Proportion of women with unexplained infertility	225 (68%)	226 (66%)	228 (67%)	0.778
Proportion of women with tubal factor	104 (32%)	114 (34%)	103 (33%)	0.778
Day 2 FSH (IU/mL)	7 ± 2.9	6.9 ± 2.9	7 ± 2.8	0.847
Day 2 estradiol (pg/mL)	30.4 ± 11.8	30.2 ± 11.9	29.6 ± 12.3	0.647
Anti-Mullerian hormone	2.4 ± 0.6	2.5 ± 0.6	2.5 ± 0.5	0.151
Antral follicle count	14.3 ± 6.4	15.6 ± 6.5	15.2 ± 6.2	0.03
Preovulatory follicle count	9.9 ± 5.6	12.3 ± 5.5	13.4 ± 5.2	<0.001
FSI	16.4 ± 2.9	22.8 ± 1.7	30.8 ± 3.7	<0.001
Oocyte retrieval	7.5 ± 4.7	9.2 ± 4.7	10.4 ± 4.7	<0.001
M2 oocytes	5.6 ± 4.2	7.1 ± 4.2	7.9 ± 4.2	<0.001
Fertilized oocytes	4.4 ± 3.6	5.8 ± 3.8	6.4 ± 3.7	<0.001
Fertilization rate	54.3 ± 25.6	59.8 ± 22.2	59.5 ± 21.4	<0.001
COH ^b days	12 ± 2.6	11.8 ± 2.4	11.8 ± 2.5	0.67
Estradiol at hCG day (pg/mL)	2239.3 ± 1280.2	2758.5 ± 1267.2	3016.4 ± 1206.9	<0.001
Starting FSH dose	218.8 ± 55.6	219.4 ± 53.2	219.5 ± 56.3	0.654
Total FSH dose	3996.2 ± 583	3460.1 ± 543.6	2931.1 ± 382.6	<0.001
Total embryos	3.5 ± 3.2	4.4 ± 3.4	5 ± 3.5	<0.001
Number of excellent quality embryos	1.7 ± 2.1	2.1 ± 2.6	2.6 ± 2.6	<0.001
Transferred embryos	1.5 ± 0.5	1.7 ± 0.5	1.7 ± 0.4	<0.001
Clinical pregnancy	0.27 ± 0.4	0.4 ± 0.4	0.57 ± 0.4	<0.001

Baseline characteristics and COH data are presented as means and standard deviations but causes of infertility and clinical pregnancy data are presented as frequencies and percentages

^a Follicular sensitivity index.

^b Controlled ovarian hyperstimulation

contrast to our results, in which the fertilization rate was found to increase in line with the FSI groups.

On the other hand, the more recent study by Hassan et al., which evaluated the role of FORT in 303 infertile women with unexplained infertility, showed that the fertilization rate increased in accordance with the FORT groups which is similar to our results [10].

When we compared pregnant and non-pregnant women, we found that FSI, retrieved oocytes, M2 oocytes, and the total number of embryos available for transfer were significantly higher in the pregnant group. Similar results were reported by Gallot et al. and Hassan et al. However, Zhang et al. did not find a significant difference between pregnant and non-pregnant women as regards the values of FORT, the number of oocytes retrieved, the total number of embryos, and the number of embryos transferred.

As outlined before, some of the results reported by Zhang et al. and Gallot et al. were different from ours. This may be explained by the difference in the studied groups of patients;

whereas we studied couples with tubal factor and unexplained infertility, Gallot et al. and Zhang et al. studied couples with different factors of infertility including women with endometriosis and couples with male factor of infertility with potentially poor quality gametes.

To evaluate the performance of FSI in predicting the clinical pregnancy as compared to other parameters, we used ROC curves which showed that FSI is a better predictor of pregnancy than are the AFC, PFC, and the total FSH dose. It had a better ROC with a higher area under the curve (0.638 vs 0.509, 0.538, and 0.589, respectively). We believe this underlines the importance of the FSI and proves that the FSI predictive value cannot be substituted by any of the components of its equation (Table 3 and Fig. 1). In fact, ROC revealed that FSI ranked second in accuracy of pregnancy prediction with area under the curve only less than that of the woman's age. It was superior to all the other predictors with a higher area under the curve (Table 3). ROC curves also showed that FSI is a better predictor of pregnancy than OSI and FORT with

Table 2 Baseline characteristics and COH data in pregnant and non-pregnant women

	Non-pregnant (<i>n</i> = 586)	Pregnant (<i>n</i> = 414)	<i>P</i> value
Age	34.6 ± 4	29.9 ± 4.6	<0.001
Gravidity	0.8 ± 0.7	0.8 ± 0.7	0.809
Parity	0.4 ± 0.6	0.4 ± 0.6	0.655
Body mass index (kg/m ²)	28.8 ± 3.1	27.3 ± 3.5	<0.001
Duration of subfertility (years)	5.4 ± 2.3	5.3 ± 2.2	0.56
Day 2 FSH (IU/mL)	7 ± 2.9	7 ± 2.8	0.787
Day 2 estradiol (pg/mL)	30.1 ± 12	30.1 ± 12	0.973
Anti-Mullerian hormone	2.5 ± 0.6	2.5 ± 0.6	0.928
Antral follicle count	14.9 ± 6.6	15.1 ± 6.2	0.662
Preovulatory follicle count	11.5 ± 5.7	12.3 ± 5.5	0.038
Follicular sensitivity index	22.1 ± 6.4	25.1 ± 6.2	<0.001
Serum estradiol on hCG day (pg/mL)	2615.7 ± 1324.5	2754.2 ± 1240.1	0.095
Retrieved oocytes	8.5 ± 4.8	9.8 ± 4.7	<0.001
M2 oocytes	6.4 ± 4.3	7.5 ± 4.2	<0.001
Fertilized oocytes	5.1 ± 3.7	6.1 ± 3.7	<0.001
Fertilization rate (percent)	55 ± 24.6	62.1 ± 20.4	<0.001
COH ^a days	11.9 ± 2.5	11.7 ± 2.5	0.186
Starting FSH doses (IU)	221.8 ± 53.7	215.7 ± 56.7	0.087
Total FSH doses (IU)	3551.8 ± 678.4	3333.3 ± 634.5	<0.001
Total number of embryos	4 ± 3.3	4.7 ± 3.4	<0.001
Number of excellent quality embryos	2 ± 2.4	2.4 ± 2.5	0.016
Number of transferred embryos	1.6 ± 0.6	1.7 ± 0.4	<0.001

Data are presented in the form of means and standard deviations

^a Controlled ovarian hyperstimulation

area under the curve of 0.595 and 0.592 for the OSI and the FORT, respectively (Table 3 and Fig. 2).

We conducted a multivariate logistic regression analysis which showed that the effect of FSI on clinical pregnancy

Table 3 Receiver operator curve results for predictors of pregnancy

	AUC ^a	Confidence interval of AUC ^a	<i>P</i> value
Follicular sensitivity index	0.638	(0.603–0.673)	<0.001
Follicle output rate	0.592	(0.557–0.627)	<0.001
Ovarian sensitivity index	0.595	(0.559–0.63)	<0.001
Antral follicle count	0.509	(0.473–0.545)	0.629
Preovulatory follicle count	0.538	(0.502–0.574)	0.042
Total FSH dose	0.589	(0.554–0.625)	<0.001
Age	0.77	0.741–0.798	<0.001
Body mass index	0.63	0.595–0.665	<0.001
Oocyte retrieval	0.57	0.534–0.606	<0.001
Fertilization rate	0.576	(0.54–0.611)	<0.001
Total number of embryos	0.573	(0.537–0.608)	<0.001
Excellent quality embryos	0.553	(0.517–0.589)	0.004
Transferred embryos	0.559	(0.523–0.549)	0.002
Anti-Mullerian hormone	0.524	(0.488–0.561)	0.187
Day 2 FSH	0.504	(0.468–0.54)	0.82

^a Area under the curve

Table 4 Logistic regression data using clinical pregnancy as the dependent variable

	Odds ratio	95% Confidence interval of odds ratio	P value
Age	0.79	(0.76, 0.81)	<0.001
Body mass index	0.91	(0.87, 0.94)	<0.001
FSI ^a	1.07	(1.05, 1.1)	<0.001
Retrieved oocytes	1.06	(1, 113)	0.042
Fertilization rate	1.01	(1, 1.02)	0.002
Total number of embryos	0.913	(0.824, 1.01)	0.08
Number of excellent quality embryos	1	(0.92, 1.08)	0.926
Number of transferred embryos	1.3	(0.86, 1.98)	0.208

^a Follicular sensitivity index

rate was independent of possible confounding factors (Table 4). Similar results were reported with FORT in the study by Gallot et al. who conducted a binary logistic regression analysis and concluded that the FORT effect on the pregnancy rate was independent from the patient's age and PFC [6]

In addition to its role in predicting the ovarian response to COH, FSI could have several other potential applications. It can be of value to guide the management of subsequent IVF/ICSI cycles, define POR, and guide the cancelation criteria in IVF/ICSI due to POR.

If IVF/ICSI failed, the management of future cycles can be guided by the patient's FSI. Women with high FSI values should receive the same doses of FSH in future cycles while those with low FSI values should receive higher doses of FSH as well as possibly considering other strategies to boost the ovarian response. This may include the use of the short agonist or antagonist protocol, the addition of LH, or the use of dehydroepiandrosterone [18].

Poor responders were defined by the Bologna criteria as those who had three or fewer oocytes with the conventional protocol. It has also considered "previous POR" as one of the criteria that define women with expected POR for IVF/ICSI [15]. However, it does not pay attention to the response of the follicles to the ovarian stimulation which is reflected by the FSI which could actually provide a more accurate definition of POR. Thus, we believe that the concept of FSI may introduce a new insight into the definition of POR.

In current practice, the criteria for canceling the cycle for POR depend on the PFC irrespective of the AFC. Thus, following the Bologna criteria, many practitioners would cancel the cycle if the PFC is <3 [19, 20]. For example, if the AFC was 3 and PFC was 2, many practitioners would agree on canceling the cycle; however, taking the total dose of FSH used into account can provide another insight; in the aforementioned example, if the total dose of FSH required was 1500 IU, the FSI would be 44.4 which means that these follicles have actually responded well and thus instead of

Fig. 1 ROC curves showing that FSI had a greater area under the curve than those of the AFC, PFC, total FSH dose, FORT, and OSI **Fig. 2** ROC curves also showed that FSI is a better predictor of pregnancy than OSI and FORT

canceled the cycle, oocyte retrieval can be considered. Evaluating the role of FSI in predicting pregnancy in women with PFC <3 is required in future research.

The study by Nicopoullos and AbdAllah included 1350 women undergoing IVF/ICSI with PFC less than 3. Women were categorized into three groups; group 1 had oocyte retrieval, group 2 canceled the current cycle and proceeded to intrauterine insemination (IUI), and group 3 canceled the cycle with subsequent attempt using different doses of gonadotropin. They noted that the clinical pregnancy rate was lower in the IUI group. However, when they compared groups 1 and 3, they reported that the clinical pregnancy rate was higher in group 1 but the difference was not significant. Thus, their conclusion was in support of proceeding with oocyte retrieval in women with PFC <3 (or in women with POR) [21]. The FSI can possibly provide useful guidance to objectively reach a decision for these women; OSI cannot provide such guidance because it can only be calculated after ovum pick up.

On the other hand, the use of FSI to determine ovarian responsiveness to exogenous gonadotropins may have some limitations in practice. In women with PCOS, the use of FSI will be limited by the high AFC. Also, in order to utilize the FSI as a predictor of ovarian response to exogenous gonadotropins, the endogenous FSH needs to be suppressed before COH; thus, it cannot be used with the short agonist or antagonist protocols.

Although it can be argued that multiplying the AFC by the total FSH doses will level out these two opposite measures of ovarian responsiveness, this argument does not acknowledge that PFC is a component of the equation. When AFC is studied as a separate variable, women with higher AFC are expected to have higher PFC, better oocyte yield, and better pregnancy rates. Conversely, when AFC is studied as a part, FSI in which the actual response of AFC to stimulation is measured. High AFC values will only result in a high FSI if it responds well to stimulation and yields a high PFC value. FSI is trying to assess the function of the growing follicles by measuring its response to stimulation but AFC alone measures a number irrespective of its function.

We concluded that FSI is an independent factor that influences the clinical pregnancy rate in IVF/ICSI cycles. Women with higher FSI had higher retrieved oocytes, fertilization rate, and clinical pregnancy in couples with tubal factor or unexplained infertility undergoing IVF/ICSI with expected normal ovarian response.

Compliance with ethical standards The study was approved by the research ethics committee of Cairo University.

Conflict of interest The authors declare that they have no conflict of interest.

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