Central Asian Journal of Medical Sciences
CAJMS

Original Article

Cent Asian J Med Sci. 2022 June;8(2):127-134. https://doi.org/10.24079/CAJMS.2022.06.007

Performance of Ovarian Response Prediction Index As Predictor of Ovarian Response

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Submitted: December 23, 2021
Revised: December 30, 2021
Accepted: June 21, 2022

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Objective: We aimed to evaluate potential predictors of response to controlled ovarian stimulation (COS), including follicle stimulating hormone (FSH), Estradiol, antral follicle count (AFC), and ovarian response prediction index (ORPI). **Methods:** In this prospective, single center study, we recruited 55 infertile women underwent the first cycle of in vitro fertilization/intracytoplasmic injection/intrauterine insemination (IVF/ICSI/IUI). We measured serum FSH and anti-mullerian hormone (AMH) level by ELISA and evaluated AFC. In accordance with formula, AMH x AFC / patient's age, ORPI was calculated. **Results:** The study participants are aged between 25 to 48 in infertility women. The mean age of the participants are 34.5 ± 5.5. The hormonal predictors, as well as ovarian response, are presented in Table 2. Predict ovarian hypo response by E2 and ORPI. Multivariable models improved the predictive accuracy for hypo-response (AUC > 0.6). With regard to the hyper-response, ORPI, E2 and AFC showed good predictors. In the multivariable model, the ORPI, E2 and AFC presented the best predictive accuracy, with an AUC 0.81, a sensitivity of 87 %, and a specificity of 67 %. **Conclusion:** ORPIndex is predicting the hyper-response more accurately than the ovarian hypo- response in infertility women. Participant's ovarian reserve biomarkers (AFC and E level) was significantly increased predictive accuracy.

Keywords: Infertility Women, Ovarian Diseases, Follicle Stimulating Hormone, Anti-mullerian Hormone, Fertilization

Introduction

Controlled ovarian stimulation (COS) is initial essential part of the in vitro fertilization (IVF) process which occurs in order to producing an optimum number of mature oocytes. Moreover, it provides preferences of the most viable embryo for fertilization [1]. But in spite of some limitation of response to COS, which covers ovarian hyperstimulation syndrome (OHSS) and inadequate response, it causes IVF cycle cancellation. In addition, response to COS is unsteady and difficult to predict [2, 3]. In

terms of OHSS, it is determined as the exaggerated reaction to excess hormone and may advance to possible complications, ascites, hypovolemia and hemoconcentration, because of the extravasation of leak fluid into abdominal cavity [4, 5].

To predict a possible response to COS, scientists have been suggested several biomarkers of ovarian response, which includes serum hormone parameters and ovaries measurements in pelvic ultrasound, during the past years [6, 7]. Follicle stimulating hormone (FSH), anti-Mullerian hormone (AMH), basal Estradiol (E2) and Antral follicle count (AFC) are mostly used as biomarkers of ovarian response. A systematic review by La Marca et al. including 305 citations of which 41 and 25 studies, respectively, reported the ability of AMH and AFC to predict response to COS. The literature review demonstrated that AFC and AMH, the most sensitive markers of ovarian reserve identified to date, are ideal in planning personalized COS protocols. These sensitive markers permit prediction of the whole spectrum of ovarian response with reliable accuracy and clinicians may use either of the two markers as they can be considered interchangeable [8] Another systematic review of Broer et al presented that summary estimates of sensitivity and specificity for AMH were 82 and 76%, respectively, and 82 and 80%, respectively, for AFC. Comparison of the summary estimates and ROC curves for AMH and AFC showed no statistical difference [9]. Oliveira and her colleagues developed a predictor index, the ovarian response prediction index (ORPI), which is affordable three variable index and it was calculated as multiplying the AMH level by the AFC and divided by the patient's age [6]. Here, a total of 129 patients enrolled in the ICSI programme included, and ORPI values were calculated by multiplying the AMH level (ng/ml) by the number of antral follicles (2–9 mm), and the result was divided by the age (years) of the patient (ORPI=(AMH x AFC)/Patient age). Based on the ROC curves, the ORPI accurately predicted a low ovarian response (< 4 oocytes retrieved; area under the curve (AUC):0.91), collection of ≥ 4 MII oocytes (AUC:0.85) and an excessive ovarian response (≥ 15 oocytes retrieved; AUC:0.89) [23]. Gupta et al. showed that ORPI was significantly correlated with AFC, AMH, oocyte, MII oocyte and Embryo (gr1+2). It has been also demonstrated that for collection of ≥ 4 MII oocytes, ORPI at cut off > 0.50 (AUC 0.86) has sensitivity and specificity of 74.1 % and 78.9 %, respectively. For probability of collection of > 6 good quality embryos, ORPI cut off should be > 0.75 with sensitivity and specificity of 72.7 % and 64.2 %, respectively [13]. Peluso et al demonstrated that the hyper-response patients were younger, with lower FSH, increased AMH, AFC, and ORPI values.

Regarding the assessment of the predictive capacity of ovarian reserve tests, none of them individually or combined showed a good predictive capacity for hypo-response. With respect to the hyper-responder group, individually AMH was the best predictor, while in the multivariable model, ORPI demonstrated the best predictive capacity. Furthermore, patients with serum AMH < 2.09 ng/mL (p25) had fewer AFC than patients with higher AMH values [15]. On the other hand, Selcuk et al showed that OSI was the ovarian response test that had the strongest relationship with the ART outcomes. The level of association between the ovarian response tests and poor ovarian response data was (in descending order): OSI, ORPI, AFC, AMH, and age (AUCOSI = 0.976, AUCORPI = 0.905, AUCAFC = 0.899, AUCAMH = 0.864, AUCage = 0.617). The overall association between OSI and poor ovarian response was significantly higher than the other parameters ($p < 0.05$). In patients with high ovarian response data, OSI had the highest association, followed by AFC and ORPI age (AUCOSI = 0.984, AUCAFC = 0.907, AUCORPI = 0.887) [11].

Despite of the numerous studies related to the possible predictors of the COS response, in clinical practice, selecting a preferred marker from these variable as predictor of ovarian response is still controversy among experts [8 - 10], so as to facilitate clinical decision-making for women undergoing in vitro fertilization (IVF. To select the most efficient test for determining the reproductive life at certain age is quite complicated due to the fluctuation of ovarian reserve level in each woman. Therefore, researchers have been proposed models with combination of several biomarkers to improve the effectiveness of ovarian response. Moreover, determining the potential predictor factors of ovarian response improves COS protocols to minimizing healthcare related costs and increase pregnancy rates in assisted reproduction treatment. By using these elements, we aimed to measure the biomarkers of ovarian reserve, for example FSH, AMH, AFC, and ORPI, as predictors of response to COS outcomes.

Materials and Methods

Research design

The study was conducted from May 2021 to April 2022 at the

National Center for Maternal and Child Health based on the Infertility and Reproductive Center. We employed prospective, single center study. The sample size was calculated within the hypothesis of proportion in an infinite population. A total of 59 patients was chosen in the study. We have chosen a confidence interval of 95, a margin of error 5 %, and predictive value 0.5 in this calculation.

Data collection method

Antral follicle count: An experienced sonographer measured the ovaries by using transvaginal ultrasonography, Samsung H60, as in before the COS procedure on second day of the menstrual cycle. The AFC was considered when follicles measured up to 10 mm.

Hormonal measurements: We collected peripheral blood samples through puncture of participants' forearm vein on the second or third day of the menstrual cycle prior to the ovarian induction. Using competition immunoassay, we evaluated FSH and Estradiol levels. We used AMH assay to measure AMH levels.

ORPI: We used the following data to calculate the ORPI index: AMH levels, AFC, and age of the patients. ORPI is calculated by multiplying the AMH serum level (ng/mL) by AFC, and the result is divided by the age [ORPI =AMH*AFC/women's age].

Procedure: The ovarian simulation procedure begins on the 2nd or 3rd day of the participants' menstrual cycle. 1. Timing intercourse: Simulation procedure begins on the 2nd or 3rd day of the menstrual cycle. b. take clomiphene citrate 50 - 150 mg for 5 days, c. Letrozole 2.5 mg orally intake for 7 days. Inject recombinant FSH (GonalF) 3 - 5 days after oral administration of clomiphene citrate 50 - 150 mg for 5 days. 2. IUI: Take clomiphene citrate 50 - 150 mg for 5 days, Letrozole 2.5 mg orally for 7 days, Inject recombinant FSH (GonalF) 3 - 5 days after oral administration of clomiphene citrate 50 - 150 mg for 5 days. 3. IVF: The procedure begins on the 2nd or 3rd day of menstrual cycle. Take clomiphene citrate 50 - 150 mg for 5 days. Letrozole 2.5 mg orally for 7 days. Inject recombinant FSH (GonalF) 3 - 5 days after oral administration of clomiphene citrate 50 - 150 mg for 5 days. 4. ICIS: Simulation procedure begins on the 2nd or 3rd day of the ICU. Take clomiphene citrate 50 - 150 mg for 5 days. Letrozole 2.5 mg orally for 7 days. Inject recombinant FSH (GonalF) 3 - 5 days after oral administration of clomiphene citrate 50 - 150 mg for 5 days.

On the 12th day after using the ovarian simulation procedure, the maternal plasma hCG is measured. A biochemical pregnancy is considered as serum hCG is measured to be more than 5 IU/L.

Ovarian response definition: Normal response was referred as 3 to 5 follicles measured greater than 14 mm following 6 days of ovarian induction. When at least 3 follicles measured up to 14 mm had developed or > 5 follicles had developed, it is considered inadequate response. According to this description, we divided study participants into 2 groups, hypo-response and hyper-response.

Inclusion criteria: We included women who underwent the first cycle of assisted reproduction treatment, aged younger than 50 and had no evidence of endocrine diseases such as hyperprolactinemia, thyroid dysfunctions, or polycystic ovary syndrome.

Exclusion criteria: Patients with endometriosis or who underwent chemo/radiotherapy were excluded from the current analysis.

Statistical analysis

We implemented descriptive statistics. Continuous variables (age) are presented as the central and variability. Continuous variables included hormonal measurements, ORPI and other variables. All continuous variables were normally distributed. The Kruskal-wallis test was used to determine the (continuous variables) difference between study 2 groups (hypo vs good vs hyper). Multiple comparison, the Dunn's test was followed after the Kruskal-wallis. Descriptive analysis of category variables was calculated as frequency and percentages. In category variables, association between study 2 groups was found by applying Pearson's chi-square test. The chi-square test was only used when the number of participants per cell was sufficient. We used a chi-square test to compare the effectiveness of ovarian response by patient's characteristics (Table 1). The confidence interval for the analysis was calculated as 95 %, and was considered statistically significant if the p value was < 0.05. In hypo and hyper-response groups, the predictive capacity of independent variables was assessed using receiver operating characteristic (ROC) curves. The association between these variables and selection of best effective predictors were based on the area under the curve (AUC) performance. A statistical package SPSS version 26.0 was used to perform the analysis.

Ethical statements

The study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the Ethical Committee of the Mongolian National University of Medical Sciences (Protocol № 2021/3-08).

Results

The study participants are aged between 25 to 48 in infertility women. The mean age of the participants are 34.5 ± 5.5 and 58.2 % were women with infertility due to tubal. Ovarian responses were 49.1 % of hypo and 23.6 % of good. The patients in the ovarian hypo and hyper-response groups did not differ from those in the good responder group in terms of age, BMI, cause of infertility. Only the period volume could affect the ovarian response (Table 1).

The participants were divided into three groups according to ovarian response (good, hypo-, and hyper-response). The hormonal predictors, as well as ovarian response, are presented in Table 2. Participant's ORPI, E2, and AFC were statistically

Table 1. General characteristics of the participants.

Variables	Ovarian Responses				p-value
	Hypo (n = 29)	Good (n = 15)	Hyper (n = 15)	Total (n = 59)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age, years	34.5 ± 6	34 ± 6.4	34.9 ± 3.7	34.5 ± 5.5	0.909
Age of first period	14.5 ± 1.7	14.3 ± 1.1	14.3 ± 1.2	14.5 ± 1.41	0.487
Menstrual cycle length	28 ± 2.7	27.4 ± 1	27.9 ± 1.2	27.8 ± 2.0	0.411
Body mass index	24.5 ± 4.1	24.2 ± 2.2	25.3 ± 3.5	24.7 ± 3.6	0.132
Mom age menopaus	49.46 ± 3.64	48.53 ± 3.29	49.221 ± 1.58	49.15 ± 3.11	0.707
Inf/duration	5.26 ± 4.73	4.29 ± 3.58	5.0 ± 3.42	4.96 ± 4.11	0.758
Pregnum (too)	1.34 ± 0.48	1.33 ± 0.49	1.53 ± 0.52	1.17 ± 0.49	0.293
Marital status	N (%)	N (%)	N (%)	N (%)	
Married	28 (96.6)	13 (86.7)	12 (80.0)	53 (89.9)	
Partner	1 (0.4)	2 (13.3)	3 (20.0)	6 (10.1)	
Job condition					
Normal	24 (85.7)	12 (80.0)	10 (71.4)	46 (80.7)	
Abnormal	4 (14.3)	3 (20.0)	4 (28.6)	11 (19.3)	
Pregnancy					
Yes	19 (65.5)	10 (66.7)	7 (46.6)	36 (61.0)	0.418
No	10 (34.5)	5 (33.3)	8 (53.4)	23 (39.0)	
Regular					
Yes	21 (72.4)	13 (86.6)	13 (86.6)	47 (79.6)	
No	8 (27.6)	2 (13.4)	2 (13.4)	12 (20.4)	
Alcohol					
No	22 (72.4)	9 (60.0)	12 (80.0)	43 (83.1)	
Yes	7 (27.6)	6 (40.0)	3 (20.0)	16 (16.9)	
Smoke					
Yes	4 (13.8)	2 (13.3)	3 (20.0)	9 (15.3)	
No	25 (86.2)	13 (86.7)	12 (80.0)	50 (84.7)	
Presurgery					
Yes	8 (38.1)	6 (54.5)	1 (50.0)	15 (44.1)	
No	13 (61.9)	5 (45.5)	1 (50.0)	19 (55.9)	

Table 2. Frequencies of 59 subjects' clinical variables.

Variables	Ager groups					*p-value
	25 - 29 (n = 10)	30 - 34 (n = 25)	35 - 39 (n = 12)	40 < (n = 11)	Total (n = 59)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age, year[a]	27.1 ± 1.20	32.56 ± 1.45	36.83 ± 1.64	43.09 ± 2.55	34.5 ± 5.42	0.000
BMI, kg	25.15 ± 4.03	24.66 ± 3.22	25.11 ± 4.45	24.82 ± 4.74	24.87 ± 3.81	0.973
FSH	7.80 ± 1.48	7.51 ± 2.61	11.52 ± 4.50	8.67 ± 3.09	8.57 ± 3.34	0.077
AMH, ng/mL[b]	8.17 ± 11.11	2.73 ± 2.38	1.42 ± 1.75	1.38 ± 0.91	3.13 ± 5.28	0.005
blh	8.32 ± 5.04	6.19 ± 2.64	6.72 ± 2.31	9.55 ± 11.94	7.25 ± 5.86	0.470
Be2	31.00 ± 17.42	34.26 ± 18.58	38.02 ± 19.30	34.31 ± 20.75	34.75 ± 18.54	0.603
P4	0.14 ± 0.13	0.25 ± 0.26	2.44 ± 5.49	0.58 ± 1.33	0.74 ± 2.61	0.254
Prl[c]	17.09 ± 7.67	22.02 ± 10.99	24.95 ± 11.34	28.79 ± 6.34	22.73 ± 10.15	0.013
Tsh	4.32 ± 3.96	2.83 ± 4.15	2.93 ± 1.42	2.47 ± 0.84	3.07 ± 3.34	0.327
Dose[d]	83.0 ± 46.24	140.73 ± 65.21	168.95 ± 94.42	154.54 ± 71.43	138.10 ± 74.35	0.022
Sti eline[e]	0.83 ± 0.25	0.82 ± 0.29	0.72 ± 0.23	0.55 ± 0.20	0.75 ± 0.27	0.004
Slh	14.71 ± 4.68	14.38 ± 16.80	6.82 ± 4.68	11.89 ± 11.41	12.39 ± 12.49	0.287
Se2	538.5 ± 501.1	681.97 ± 586.62	933.85 ± 655.04	823.7 ±	729.14 ± 627.14	0.186
Sp4	0.32 ± 0.29	0.64 ± 0.49	2.74 ± 5.33	0.96 ± 1.27	1.07 ± 2.56	0.202
hcginject	11.3 ± 3.05	12.04 ± 2.41	11.91 ± 1.67	11.91 ± 1.04	11.86 ± 2.15	0.657
hcg1	27.58 ± 33.98	21.77 ± 58.34	9.79 ± 22.04	1.04 ± 3.12	15.89 ± 42.22	0.102
hcg2	56.03 ± 73.82	103.31 ± 235.24	15.58 ± 39.45	2.82 ± 9.04	56.99 ± 162.80	0.159
AMH/ Age ratio[f]	30.59 ± 41.45	8.48 ± 7.44	3.91 ± 4.87	3.25 ± 2.23	10.4 ± 19.8	0.002

*Kruskal-Wallis test. Multiple comparison test: [a]Age group 25-29 vs. 40<, p-value 0.001; [b]Age group 25-29 vs. 35-39, p-value 0.040; [c]Age groups 30-34 vs. 40<, p-value 0.000; [d]Age groups 25-29 vs. 30-34, p-value 0.021; [e]Age groups 25-29 vs. 35-39, p-value 0.004; [f]Age groups 30-34 vs. 40< , p-value 0.002.

Table 3. Clinical characteristics of the participants by ovarian responses.

Variables	Ovarian Response				*p-value
	Hypo (n = 29)	Good (n = 15)	Hyper (n = 15)	Total (n = 59)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
FSH	8.27 ± 2.69	8.55 ± 3.49	9.15 ± 4.35	8.57 ± 3.34	0.427
AMH	3.59 ± 6.98	2.95 ± 3.56	2.40 ± 2.08	3.13 ± 5.28	0.475
blh	7.54 ± 7.83	7.79 ± 3.53	6.15 ± 2.26	7.25 ± 5.86	0.512
Be2	34.19 ± 17.54	26.00 ± 18.21	44.59 ± 17.01	34.75 ± 34.75	0.168
P4	0.70 ± 1.97	0.21 ± 0.20	1.34 ± 4.45	0.74 ± 2.61	0.549
Prl	23.53 ± 10.21	20.54 ± 10.39	24.04 ± 10.20	22.73 ± 22.73	0.813
Tsh	2.88 ± 2.65	3.65 ± 4.83	2.59 ± 1.68	3.07 ± 3.33	0.941
Dose[a]	107.41 ± 59.54	131.83 ± 77.88	201.67 ± 57.83	138.10 ± 74.34	0.000
Sti eline	0.80 ± 0.32	0.67 ± 0.20	0.74 ± 0.23	0.75 ± 0.27	0.375
Slh	13.97 ± 10.32	14.70 ± 17.04	7.03 ± 10.04	12.39 ± 12.48	0.113
Se2[b]	467.37 ± 511.95	798.88 ± 613.24	1165.45 ± 614.79	729.13 ± 627.13	0.000
Sp4	1.56 ± 3.57	0.60 ± 0.59	0.56 ± 0.37	1.07 ± 2.56	0.179

Continued

hcginject	11.48 ± 2.71	12.86 ± 1.18	11.6 ± 1.29	11.86 ± 2.16	0.609
hcg1	9.31 ± 22.45	29.03 ± 73.29	15.04 ± 25.30	15.89 ± 42.21	0.525
hcg2	36.04 ± 110.73	122.27 ± 272.79	30.81 ± 60.61	56.99 ± 162.81	0.852

* Kruskal-Wallis test. Multiple comparison test: [a]Hypo vs. Hyper, p-value 0.000; [b]Hypo vs. Good, p-value 0.031.

Table 4. Ovarian reserve biomarkers and ovarian response.

Variables	Ovarian response				*p-value
	Hypo	Good	Hyper	Total	
FSH	8.29 (2.78)	8.8 (3.69)	9.15 (4.35)	8.65 (3.44)	0.738
LH	7.67 (8.12)	7.75 (3.78)	6.16 (2.26)	7.28 (6.06)	0.711
E2[a]	35.39 (17.23)	25.92 (17.65)	44.59 (17.01)	35.66 (18.23)	0.023
P4	0.74 (2.04)	0.18 (0.15)	1.34 (4.45)	0.77 (2.7)	0.535
AMH	3.62 (7.22)	2.88 (3.63)	2.4 (2.08)	3.11 (5.43)	0.778
ORPI[b]	0.78 (1.53)	0.86 (1.57)	1.02 (0.62)	0.76 (1.35)	0.045
AFC[c]	6.78 (3.45)	5.92 (2.5)	8.13 (2.95)	6.95 (3.16)	0.036

FSH – Follicle stimulation hormone, LH – Luteinizing hormone, E2 – Estradiol, P4- Progesterone, AMH – Anti-muller hormone, ORPI – Ovarian response prediction index, AFC – Antral follicle count. * Kruskal-Wallis test. Multiple comparison test: [a]Hypo vs. Good, p-value 0.004; [b]Hypo vs. Hyper, p-value 0.009; [c]Hypo vs. Hyper, p-value 0.049.

Table 5. Predictor's AUC analysis for predicting ovarian hypo-response.

Univariable model	AUC	95% CI	SE	SP	p-value
AFC	0.58	0.25- 0.67	0.45	0.58	0.192
E2	0.69	0.51- 0.87	0.89	0.91	0.063
ORPI	0.59	0.40- 0.76	0.78	0.75	0.395
Multivariable model	**AUC**	**95% CI**	**SE**	**SP**	
AFC + E2	0.68	0.51- 0.86	0.81	0.76	0.059
E2 + ORPI	0.67	0.47- 0.87	0.88	0.66	0.100
ORPI + AFC + E2	0.73	0.56- 0.89	0.92	0.75	0.022

E2 – Estradiol, ORPI – Ovarian response prediction index, AFC – Antral follicle count, CI – Confidence interval, SE – Sensitive, SP – Specific

Table 6. Predictor's AUC analysis for predicting ovarian hyper-response.

Univariable model	AUC	95% CI	P	SE	SP
AFC	0.75	0.25; 0.67	0.192	0.45	0.58
E2	0.56	0.14; 0.65	0.063	0.89	0.91
ORPI	0.71	0.40; 0.64	0.395	0.78	0.75
Multivariable model					
AFC + E2	0.68	0.62; 0.76	0.059	0.83	0.73
E2 + ORPI	0.67	0.58; 0.79	0.100	0.87	0.69
ORPI + AFC + E2	0.81	0.72; 0.89	0.021	0.87	0.67

E2 – Estradiol, ORPI – Ovarian response prediction index, AFC – Antral follicle count, CI – Confidence interval, SE – Sensitive, SP – Specific

significantly different in the three groups of ovarian responses (p = 0.045, 0.023, 0.036) (Table2).

In our study, AMH and FSH did not significantly differ between the three groups of ovarian responses. Figure 1.2

shows the results of the ROC analysis of potential variables (AFC, Estradiol, ORPI) to predict ovarian response. Hormonal measurements and ORPI results predicting ovarian response are shown in Tables 3 and 4.

Predict ovarian hypo response by E2 and ORPI. Multivariable models improved the predictive accuracy for hypo-response. The combined model of ORPI, E2 and AFC showed a better predict to poor response, with AUC 0.73, the sensitivity of 92 %, and specificity of 75 % (Table 3).

With regard to the hyper-response, ORPI, E2 and AFC showed good predictors. In the multivariable model, the ORPI, E2 and AFC presented the best predictive accuracy, with an AUC 0.81, a sensitivity of 87 %, and a specificity of 67 % (Table 4). The ORPI+AFC+E2 is the most sensitive model to predicting ovarian hypo-response ($p = 0.022$) in Table 5.

Discussion

In regard of the predictive ability of hyporesponse, if an AUC approximately 0.5 illustrates a test without discriminating ability, there has no result of good accuracy in biomarkers [12]. According to the several study results, the prevalence of inadequate response fluctuates between 5.6 % and 35.1 %. Moreover, AMH cut-off value ranging between 0.7 and 0.75 ng/mL predicts poor ovarian response. In present study the mean serum AMH for hypo-response was 3.62 ng/mL. High risk of cycle cancelation mainly occurs in the study participants measured their AMH level very low (0.1 – 0.35 ng/mL). Interests related to reliability of multiple assays have been growing among experts because AMH assays were differently used in these studies. Oliveira and colleagues demonstrated that ORPI showed an excellent ability to predict low ovarian response and it seemed to be superior to the other ovarian reserve. In fact, there has been issue whether AMH could be considered a reliable marker of IVF outcomes. Several studies determined a correlation between AMH and pregnancy whereas others did state a positive correlation [16 - 19]. A prospective cohort study conducted on 84 infertile couples' candidate for Intracytoplasmic sperm injection (ICSI) by Amin et al showed that women with poor response were statistically older than those with normal ovarian response (33.1 ± 5.9 vs. 29.8 ± 5.4, respectively). The number of cumulus (12.1 ± 5.2 vs. 2.5 ± 1.5), MII oocytes (7.8 ± 3.6 vs. 2 ± 0.8), grade A embryos (3 ± 0.8 vs. 1.4 ± 0.9) and total number of embryos (3.8 ± 2.2 vs. 1.7 ± 0.7) were significantly higher in normal responders. ORPI has the highest accuracy in predicting ovarian response (88 %) when compared to AMH (83 %) and AFC (86 %). AMH, AFC and ORPI are good predictive of the ovarian response and help in choosing the protocol and gonadotropin dose of induction and prediction of OHSS [20]. Moreover, Haritha et al presented that there was a positive correlation of ORPI with MII oocytes and total number of oocytes. Regarding the probability of collecting ≥ 4 oocytes under the ROC curve, the AUC for ORPI is 0.68 (95 %CI 0.65 - 0.72) with sensitivity of 78.4 and specificity of 51.4 for a cut off of > 0.44. For collecting ≥ 15 oocytes ROC curve had an AUC of 0.72 with sensitivity of 66.7 and specificity of 73.4 for a cut off of > 1.28. In a patient undergoing IVF treatment, ORPI has a poor ability to predict retrieval of ≥ 4 oocytes or ≥ 4 MII and fair ability for hyper response with ≥ 15 oocytes. ORPI can serve as a counselling tool for predicting ovarian response [21]. According to the findings of Oliveira et al, ORPI can predicts an excessive response with a predictive capability higher than each marker individually. While good predictors of high response were AFC, AMH, and ORPI and best biomarker was AFC as stated in Ashrafi et al. study. The results of our study are similar, and it is possible to predict ovarian response using E2, AFC, and ORPI.

The strength of our study was that the patient was evaluated following up on time. However, some of the women in the study had undergone infertility treatment, which may have impacted the results of the study. Furthermore, our study had limited sample size and clinical pregnancy rate was not taken in outcome analysis. Therefore, in the future, more well-designed and sufficient sample size included studies are needed in order to determine good predictors for ORPI and assess the results of pregnancy and delivery outcomes.

Conclusion

The ORPI can be used to predict ovarian response. This is predicting the hyper-response more accurately than the ovarian hypo- response in infertility women. Participant's ovarian reserve biomarkers (AFC and E level) was significantly increased predictive accuracy.

Conflict of interest

The authors declared no conflicts of interest.

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