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FORT: Predicting IVF/ICSI Outcomes

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A B S T R A C T

Background:The study focused on evaluating the Follicular Output Rate (FORT) as a prognostic indicator for how well a patient responds to Follicle-Stimulating Hormone (FSH) during ovarian stimulation in IVF/ICSI cycles and its association with reproductive outcomes. The study involved calculating the FORT for a cohort of 138 women undergoing IVF/ICSI. FORT was determined by comparing the number of pre-ovulatory follicles at the time of hCG administration to the initial antral follicle count (AFC) before stimulation. The accuracy of FORT as a prognostic indicator was evaluated by comparing it with actual reproductive outcomes, such as the number of mature oocytes retrieved, quality of oocytes, number of embryos, chemical and clinical pregnancy rates. ***Result*:** The mean age (±SD) of the women was 31.36 years (± 3.28 years), the mean FORT was 53.453. Based on FORT values, study population was divided into three groups, those with low (≤42), medium (>42 to 58) or high FORT (>58). Those with Positive pregnancies had much higher FORT levels (74.025) than those with Negative pregnancies (38.975) and this result was statistically significant. FORT and number of mature oocytes (MII) retrieved were positively correlated and the number of oocytes and embryos obtained increased progressively from the low to the high FORT groups. ***Conclusion*:** The study found that FORT is a reliable and accurate indicator of ovarian response to FSH. A higher FORT correlates with a better response to FSH, leading to more mature follicles and higher quality oocytes.

Keywords: FORT, IVF/ICSI, Chemical pregnancy, Clinical pregnancy.

INTRODUCTION

FORT is a metric used to assess the efficiency of the ovarian response to stimulation. It is calculated as the ratio of the number of pre-ovulatory follicles (those that are mature and ready for retrieval) to the antral follicle count (AFC) at the start of the stimulation cycle.

FORT = (Number of pre-ovulatory follicles / Antral Follicle Count) × 100

It reflects the ability of the ovaries to convert the pool of small, antral follicles into larger, mature follicles that are capable of yielding viable oocytes. It provides a more dynamic assessment of ovarian function compared to static measurements like AFC or serum hormone levels alone.

Genro*et al*., proposed the concept of the follicular output rate (FORT) in 2011 [1]. The study by Gallo*et al*., (2012) highlighted the importance of FORT as a useful and quantitative indicator of both ovarian response and potential pregnancy outcomes in women undergoing fertility treatments. The positive correlation between higher FORT and improved pregnancy rates provided valuable insight into the role of FORT in reproductive medicine, suggesting that it could be a key factor in optimizing fertility treatment strategies [2]. Hassan *et al*.,'s findings underscored the significance of FORT in predicting IVF/ICSI outcomes, particularly in patients with unexplained infertility. The study highlighted that higher FORT was associated with more high-quality embryos and higher clinical pregnancy rates [3]. The findings of Yang H *et al*., also showed that FORT is a powerful tool for measuring ovarian reactivity [4].

The present investigation aimed at testing the possible relationship between the FORT and the reproductive competence of antral follicles as reflected by the outcome of oocytes and embryos obtained in IVF-ET cycles.

Materials and methods

We prospectively studied 138 patients, ranging from 26 to 45 years of age, who underwent COH for IVF + embryo transfer (ET) from December 2022 to December 2023. All of the patients met the following inclusion criteria: Both ovaries were present, without any morphological abnormalities, and seen adequately on transvaginal ultrasound. The exclusion criteria were: current or past diseases affecting the ovaries, clinical and/or biological signs of hyperandrogenism, diagnosis of polycystic ovarian syndrome.

Local institutional review board approvals for the use of clinical data for research studies were obtained and written informed consent was obtained from all patients.

The antral follicle size and count assessments were performed with 7.5 to 10 MHz transvaginal probe sonoscape, on Day 2/3 of cycle. Baseline AFC count was recorded .Patients were submitted to controlled ovarian hyper stimulation from day 2/ day 3. The gonadotrophin FSH was started in dose of 225 IU. Follicular monitoring was done from day 6, whenever 1 follicle was found to be in size more than 14mm, antagonist injection cetrorelix 0.25mg subcutaneously was added daily. Follicle monitoring was continued. When more than 2 preovulatory follicles were seen, Follicular Output Rate (FORT) was calculated according to formula given below.

$$\text{FORT} = \frac{\text{Number of pre ovulatory follicles on HCG day}}{\text{number of AFC at baseline}} \times 100$$

10000 IU Human Chorionic Gonadotropin was administered as soon as more than 2 preovulatory follicles (16 to 22mm in diameter) were seen. Oocytes were retrieved by transvaginal ultrasound guided aspiration 36 hrs after HCG administration. Then, number and grading of oocytes was calculated. Number of embryos formed and quality of embryos were noted. Embryo transfer was performed on day 3/5 according to embryo development. Beta HCG was done after 15 days. Chemical pregnancy, which is a positive urinary pregnancy test was noted. Clinical pregnancy, defined as presence of intrauterine embryo with cardiac activity at around 6 weeks after treatment was noted.

Mean and standard deviation were used to describe quantitative data, and frequency and percentage will be used for qualitative data. The relationship between two continuous variables was assessed by a correlation analysis when they were independent from each other and by regression when there was a dependent relationship between the variables. Spearman's test was used to determine if the correlation coefficients (r) were significantly different from zero. The level of significance was kept 95% for all statistical analysis.

RESULTS

Overall population, COH characteristics and IVF-ET results

At the time of inclusion, women were aged 31.36 ± 3.28 years and presented BMI values at 21.38 ± 1.39 kg/m^2. At baseline, AFC was at 11.29 ± 3.73 follicles and mean AMH was 2.39±1.29. Overall, FORT was 53.45±19.83. An average of 5.45±2.80 oocytes were retrieved, 3.95± 2.11 embryos were obtained and clinical pregnancy rate was 31.15%.

Table 1: The demographic and reproductive data

Variable	Mean ± SD
Age	31.36 ± 3.28
FORT (Follicular Output Rate) (%)	53.45±19.83
Total AFC (antral follicle count)	11.29 ± 3.73
Number of oocytes retrieved	5.45± 2.80
Number of embryos formed	3.95± 2.11
BMI (body mass index) Kg/m^2	21.38±1.39
AMH (anti-Mullerian hormone) ng/ml	2.39 ±1.29

Based on FORT values, study population was divided into three groups as shown in table 2, those with low (≤42), medium (>42 to 58) or high FORT (>58).

Table 2: Follicular Output Rate (FORT)

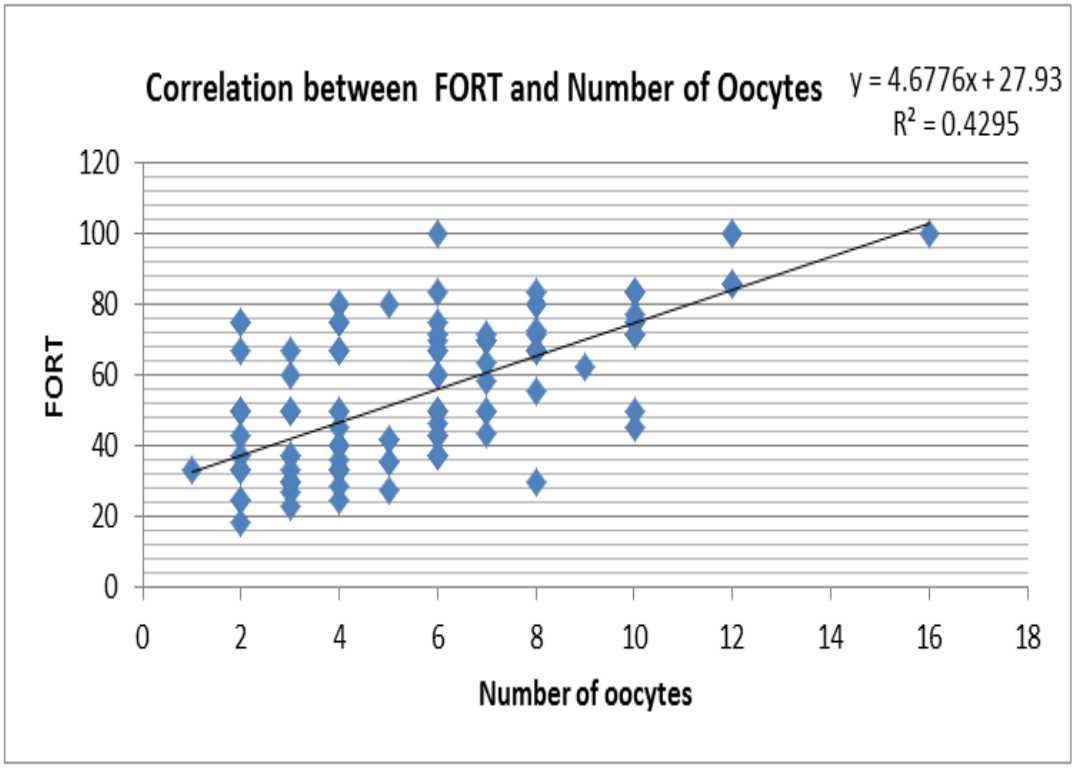
	Range	Number of cases	Percentage
Low FORT	0 to 42	56	40.57%
Medium FORT	>42 to 58	26	18.84%
High FORT	>58	56	40.57%
		Total = 138	100%

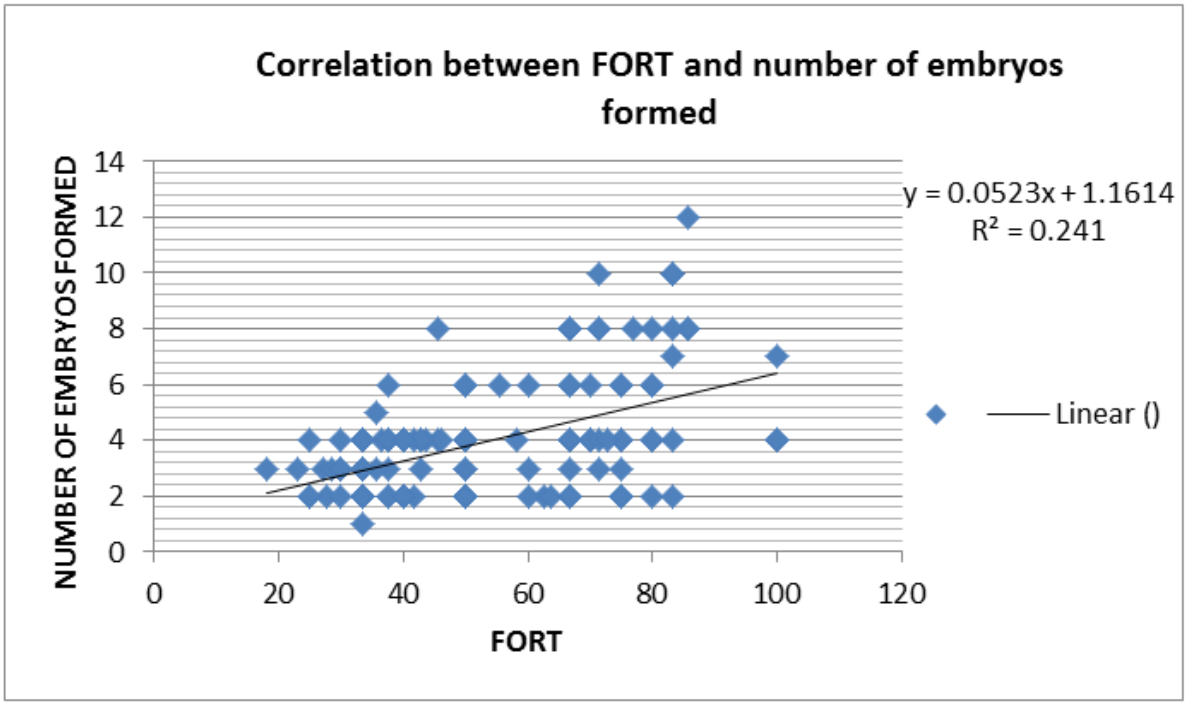
Mean Value: 53.453, Standard Deviation: 19.838

The correlation between FORT and other related variables is shown in Table 3. Based on this table, there was a significant correlation between FORT and number of oocytes retrieved and number of embryos formed ($P < 0.05$). Other related variables (BMI, age, AMH) had no significant correlation with FORT ($P > 0.05$).

Table 3: Correlation of FORT with other related variables

Variables	Correlation coefficient	P value
Age	0.013	0.879
BMI	-0.011	0.890
AMH	0.035	0.682
Number of oocytes	0.655	<0.001
Number of embryos	0.0053	<0.001

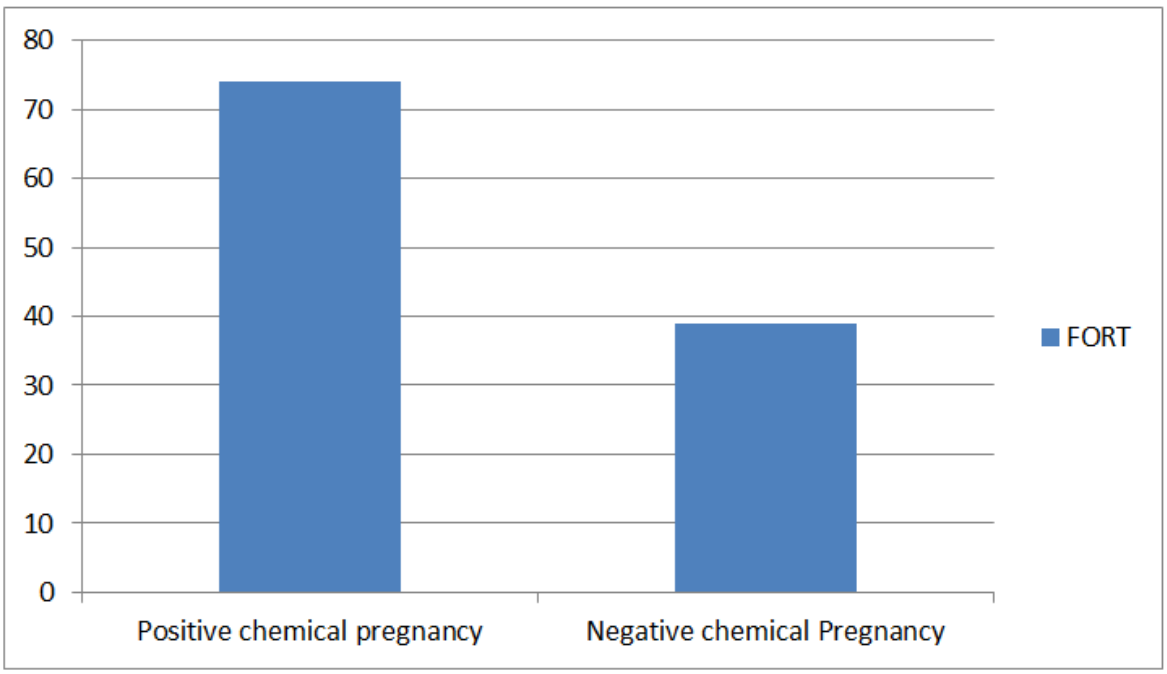




As shown in Table 4, FORT levels varied significantly between Negative and Positive Chemical Pregnancy groups ($p < 0.001$). Those with Positive pregnancies had much higher FORT levels (74.025) than those with Negative pregnancies (38.975). This suggests FORT might be useful for predicting pregnancy outcomes. Higher FORT was associated with higher chances of positive pregnancy outcomes.

Table 4: Distribution of FORT according to Chemical Pregnancy

Chemical Pregnancy	Mean FORT	N	Std. Deviation	T value	P value
Negative	38.975	81	8.488	-20.887	p<0.001
Positive	74.025	57	11.218		
Total	53.453	138	19.838		



DISCUSSION

Key finding from this investigation is the relationship between the Follicular Output Rate (FORT) and IVF-ET (in vitro fertilization and embryo transfer) outcomes. The study found that a higher proportion of FSH (follicle-stimulating hormone)-responsive antral follicles correlates with better pregnancy outcomes, independent of factors like age and follicle counts before and after controlled ovarian hyperstimulation (COH). FORT and number of mature oocytes (MII) retrieved were positively correlated and the number of oocytes and embryos obtained increased progressively as the Follicular Output Rate (FORT) moved from low to high groups. This suggests that higher FORT values, which indicate better ovarian responsiveness to stimulation, are associated with more favorable outcomes in terms of oocyte yield and embryo production.

Thus, FORT could serve as a promising qualitative marker for assessing the health and functionality of antral follicles. Additionally, the study supports the idea that lower responsiveness of antral follicles to FSH might indicate some level of dysfunction in the follicles or oocytes.

Consistent with our results there were several studies. Gallot*et al*.,showed the number of oocytes and embryos obtained increased progressively from the low to the high FORT groups ($P< 0.001$), but fertilization rates remained steady. The overall percentage of patients who underwent ET was lower in the low FORT group when compared with the remaining groups. Clinical pregnancies in low, medium and high FORT groups were 33.3%, 51.2%, 55.7% respectively. A decreased prevalence of top-morphology embryos was observed in the low when compared with the high FORT groups. FORT levels were slightly yet significantly correlated ($r = 0.14$; $P< 0.02$) with the percentage of top-morphology embryos [2].

Similarly Zhang *et al*., observed in a larger cohort of 1,503 non-PCOS patients that the number of retrieved oocytes and total number of embryos progressively increased from the low to high FORT groups ($p < 0.001$). Mean FORT was of 65% [5].

Rehman*et al*., also found there was a positive relationship between FORT and clinical pregnancy rates (35.8%), and FORT values were higher in pregnant compared to non-pregnant patients (64.2 vs. 49.3%, respectively, $p = 0.0001$) [6].

Hassan *et al*., reported similar results in a prospective study on 303 women undergoing IVF/ICSI for unexplained infertility. Patients were divided into three groups according to FORT: low FORT ($n = 97$), below the 33rd percentile, moderate FORT ($n = 104$) with values between the 33rd and the 67th percentiles, and high FORT ($n = 102$), above the 67th percentile. There was a progressive and significant increase from low to high FORT groups regarding number of retrieved oocytes (5.4 ± 1.5, 6.8 ± 2.8, and 7.4 ± 2.1, respectively; $p < 0.001$), clinical pregnancy rates (29.9, 43.3, and 57.8%, respectively; $p < 0.001$), and fertilization rates (48.4% ± 21.8 vs. 55.3% ± 20.3 and 57.4% ± 19.2, respectively; $p = 0.006$). Multivariate logistic regression analysis revealed that the correlation between FORT and pregnancy was independent of potential confounding factors ($p = 0.008$) [3]. Grynberg*et al*., also showed similar results in a systematic review and meta analysis [7].

CONCLUSION

Follicular Output Rate (FORT) is a critical tool for managing hypo-responders in Assisted Reproductive Technology (ART). FORT provides a quantitative and qualitative index that can guide treatment decisions, particularly for those with impaired sensitivity to Follicle-Stimulating Hormone (FSH). By considering FORT, healthcare professionals can tailor treatment protocols, choose appropriate gonadotropins, and adjust stimulation doses to improve outcomes for hypo-responders in ART.

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