

Kristian Galea: kjsg2@cam.ac.uk; Alka Prakash: Alka.Prakash@addenbrookes.nhs.uk; Tulay Karasu: Tulay.Karasu@addenbrookes.nhs.uk

1. Introduction

Understanding the parameters which affect the outcome of assisted reproductive technologies (ARTs) such as in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI) has long been the subject of research. The identity of and extent to which these variables determine success rates is important to delineate so that clinicians may offer predictions and optimise treatment.

IVF and ICSI protocols involve ovarian stimulation which is accomplished with gonadotropins. Optimal stimulation results in multiple ovulation which allows the retrieval of mature oocytes and the development of viable embryos. The dosage of gonadotropins that produce this outcome is determined in a patient-specific manner and is typically dependent upon the protocols at the fertility clinic and the clinician’s experience.

While previous studies have attempted to create models which predict outcomes for patients undergoing ART, these cannot always be generalised to all IVF clinics due to factors such as demography and public funding.

Therefore, in order to ascertain a greater understanding of the factors affecting the success of fertility treatments at Cambridge IVF specifically, data from a cohort of patients who had received treatment at the clinic were analysed. In this way, it was hoped that the results would be relevant and useful for the clinicians at Cambridge IVF and would ultimately be beneficial for future patients who undergo treatment at the clinic.

2. Method

A retrospective cohort study was conducted in a university-affiliated assisted reproduction unit to assess how prediction and optimisation could occur given the demography of the patients served by the clinic. To this end, a database of 124 egg retrievals that took place as part of IVF and ICSI cycles over a six-month period was compiled from the online database, IDEAS, and from paper notes. The antral follicle count (AFC) was of particular interest as it has been identified as a good predictor of IVF success. Therefore, patients were divided into four groups according to AFC (4-9; 10-14; 15-20; 20+ and PCO). The data was then analysed using one-way analyses of variance, Kruskal-Wallis tests and chi-squared tests followed by post-hoc testing to determine statistically significant differences between the groups.

3. Results

Characteristic	AFC				Test	Test Value	P Value
	4-9 (n = 31)	10-14 (n = 28)	15-20 (n = 28)	>20 (+PCO) (n = 37)			
Age (years), mean±SD	37.26 ± 3.60 ^a	36.64 ± 4.83 ^a	35.46 ± 4.30	33.00 ± 3.34 ^b	One-way ANOVA	7.571	< 0.001
BMI (kg/m²), mean±SD	23.20 ± 4.21	23.89 ± 4.20	24.84 ± 4.14	25.26 ± 5.03	One-way ANOVA	1.386	0.250
AMH (pmol/L), mean±SD	7.26 ± 5.05	11.00 ± 4.10	18.26 ± 11.10	35.51 ± 23.44	Kruskall-Wallis	73.353	< 0.001
Total FSH Dose (IU), mean±SD	4337.90 ± 1363.83	3604.46 ± 1297.38	2259.38 ± 1048.99	1636.82 ± 508.01	Kruskall-Wallis	68.388	< 0.001
Estradiol (pmol/L), mean±SD	8807.67 ± 3552.71	10092.84 ± 5009.45	8780.33 ± 4727.67	11464.94 ± 7777.01	Kruskall-Wallis	3.539	0.316
Progesterone (nmol/L), mean±SD	3.78 ± 1.32	3.67 ± 1.28	3.10 ± 1.40	3.00 ± 1.02	Kruskall-Wallis	5.606	0.132
Endometrial Thickness (mm), mean±SD	9.32 ± 2.89	9.84 ± 2.21	9.82 ± 1.79	10.19 ± 2.48	One-way ANOVA	0.722	0.541
Days Stimulated, mean±SD	11.84 ± 2.54	11.07 ± 1.44	9.75 ± 1.38	10.59 ± 1.79	Kruskall-Wallis	16.768	< 0.001
Total Follicles Stimulated, mean±SD	11.78 ± 4.72	16.64 ± 7.00	21.92 ± 8.64	31.80 ± 14.71	Kruskall-Wallis	53.305	< 0.001
FORT (%), mean±SD*	36.47 ± 27.03	24.60 ± 11.06	18.64 ± 13.53	11.47 ± 9.60	Kruskall-Wallis	26.302	< 0.001
Eggs Retrieved, mean±SD	6.90 ± 4.04	8.43 ± 5.34	11.14 ± 5.12	15.65 ± 7.68	Kruskall-Wallis	33.417	< 0.001
Mature Eggs (MII), mean±SD	6.71 ± 3.69	7.69 ± 6.10	8.89 ± 4.30	11.17 ± 5.09	Kruskall-Wallis	9.675	0.022
Total Embryos Transferred, n (%)	21 (67.7)	20 (71.4)	21 (75.0)	21 (56.8)	Chi-squared	2.819	0.420
Positive hCG Test, n (%)	9 (32.1)	10 (38.5)	8 (29.6)	10 (29.4)	Chi-squared	0.670	0.880

4. Discussion

There was a statistically significant difference between the AFC groups as established above with regard to the following parameters: age, anti-Müllerian hormone (AMH) level, follicle-stimulating hormone (FSH) dose, days stimulated, number of follicles stimulated, number of eggs retrieved, and number of mature (MII) eggs obtained. However, surprisingly, there was no difference between the groups regarding the ongoing pregnancy rate. Furthermore, the follicular output rate (FORT) was significantly higher in those with a lower AFC. FORT is a marker of follicular responsiveness and is normally calculated as the ratio between the number of preovulatory follicles between 16-20 mm on hCG day and the AFC. This study uses a modified version of this equation to account for data collection techniques (see *).

7. Key References

- Liao *et al.* (2019) Prediction of in vitro fertilization outcome at different antral follicle count thresholds combined with female age, female cause of infertility, and ovarian response in a prospective cohort of 8269 women
- Poulain *et al.* (2021) Impact of Ovarian Yield-Number of Total and Mature Oocytes Per Antral Follicular Count-On Live Birth Occurrence After IVF Treatment
- The Eshre Guideline Group On Ovarian Stimulation (2020) ESHRE guideline: ovarian stimulation for IVF/ICSI
- Zhang *et al.* (2019) Discordance between antral follicle counts and anti-Müllerian hormone levels in women undergoing in vitro fertilization

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$$FORT = \frac{(Preovulatory\ follicles > 17\ mm) \times 100}{Antral\ follicle\ count}$$

5. Limitations

- In an effort to utilise the most recent data available at the clinic, this study selected patients who underwent IVF or ICSI in a six-month period between 2/6/21 and 3/12/21. However, this represents a period that was highly impacted by the Covid-19 pandemic. As a consequence, the cohort of patients who sought treatment during this time may be misrepresentative. It is unclear how or if this had an effect on the findings of the study.
- This study collected 44 variables per patient and there were inevitably missing data. This had the effect of reducing the power of the study and decreased the size of the cohort which could be analysed.

6. Conclusions

- This analysis supports that AFC can be a key factor in IVF and ICSI success given its correlation with multiple other relevant parameters which are predictive of success such as age and AMH level.
- Within the context of Cambridge IVF:
 - Patients with a lower AFC had a higher FORT. This is perhaps testament to clinically-intuited patient-specific stimulation methods at Cambridge IVF which avoid ovarian hyperstimulation in those with high ovarian reserve but adequately stimulate those with low reserve.
 - Although AFC is usually correlated with IVF and ICSI success, pregnancy rates at Cambridge IVF seem to be independent of AFC as the difference in ovarian reserve between the groups is offset by the difference in FORT

The information collected from this study can be considered in future when attempts are made to further optimise treatment or better predict a patient’s likelihood of success.