

Factors Affecting the Success Rate of Artificial Fertilization

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Abstract: ***Aim:** To investigate the various factors affecting the real as well as the theoretical collective live birth rates behind artificial reproductive therapy (ART). **Patients and Methods:** Retrospective study of 104 couples that underwent either an IVF or ICSI cycle between 2013 and 2014, at an infertility clinic. Data collected was analyzed by SPSS. **Results:** The success rate was 18.7%, various factors had an effect on the outcome. **Discussion and Conclusion:** There are modifiable and non-modifiable factors. Modifiable factors influencing the success rate of IVF have to be optimized before the procedure to achieve higher success rates.*

Keywords: Factors success fertilization

1. Introduction

It has been more than 30 years since the first child born after In Vitro fertilization (IVF). Since then IVF and other assisted reproductive technologies (ARTs) have advanced remarkably. Although over the past two decades there has been an increase in pregnancy rates^[1]. Yet the number of live births has still not reached the desired levels^[1]. The main aim of IVF treatment is to succeed a term live birth. For this reason, it is crucial to know the factors influencing the success of IVF not only for the decision of the patient to begin treatment, but also for determining the treatment protocol to be selected. There are numerous factors involved such as the age and weight of the woman undergoing the selected treatment protocol^[1]. There are also other reasons for infertility such as the date of her last menstrual cycle, the women's hormone levels (FSH, LH, TSH and Prolactin), Number of follicles, whether it's primary or secondary infertility and any medications she used.

2. Material and Methods

This was a retrospective study of 131 couples that underwent an artificial reproductive therapy (ART) cycle between 2013 and 2014. Out of a total of 131 cases in the mentioned period, the complete set of data was found for 104 patients. ACOG guidelines were used to define infertile patients, which are failure of conception after a year of unprotected sexual intercourse in a female below 35 years of age, or 6 months in those over 35 years.

The data collection sheet used in the study included the age, weight in KG and height in CM from which the body mass index (BMI) was calculated, hormonal profile (FSH, LH, Prolactin, TSH), medication regimen, ovarian size and number of follicles from ultrasound (US) reports and a pregnancy test for each patient. The collected factors related to conception results were analyzed by SPSS. The age was between 17-49. 38.4% have normal weight (BMI= 15-24.9), and 61.6% are overweight (BMI= >25).

Laboratory pregnancy rates in women with different age, BMI, medication regimen, hormonal profile and different number of follicles were compared. The clinical outcomes of stimulation with gonadotropin releasing hormone (GnRH)

agonist long protocol, GnRH agonist short protocol and GnH antagonist protocol were evaluated in infertile patients. Treatment regimen and Progression of pregnancy post 20 weeks were excluded from the study as well as male factors.

3. Results

As Table 1 shows the characteristics of our sample. The majority of our sample were women aged less than 50 years old (76%), while one quarter were aged 40 years old or above. Regarding infertility, 58.7% of the sample suffered from primary infertility while 41.3% had secondary infertility. Duration of infertility ranged from 1 year to 24 years with a mean of 6.98 years. When measuring the number of follicles found, the majority of the sample (78.3%) were found to have more than 5 follicles in both ovaries, while only 21.7% had less than 5 follicles and the mean number of follicles found was 8.68 follicle. When measuring the largest follicle found in each patient, the mean size of the largest follicle was found to be 27.63mm with the majority of the sample (87.5%) found to have a largest follicle size of more than 15mm, while only 12.5% of the sample found to have a largest follicle size of less than 15mm. Almost two thirds of the sample (61.6%) were found to be over the normal weight with a BMI more than 25, while 38.4% were found to be within the normal weight with a BMI between 18.5-24.9. When measuring the success rate by doing a pregnancy test, 18.7% of the patients had a positive pregnancy test, while 81.3% had a negative pregnancy test. Hormone panel was done for each patient and the following hormones were measured: Estradiol, Follicular Stimulating Hormone(FSH), Luteinizing Hormone(LH), Prolactin and Thyroid Stimulating Hormone(TSH). The mean measurements found for each hormone were as follows: Estradiol had a mean of 3620.55, FSH was 8.89, LH was 9.09, Prolactin was 436.14 and TSH was 3.03.

As displayed in Table 2, the relationship between the number of follicles found and factors that can affect it. When comparing the number of follicles between our two age groups, women who were less than 40 years old were found to have more than 5 follicles (78.9%) more often than having less than 5 follicles (21.1%). A similar result was observed in women who were 40 years old or older with

20% having less than 5 follicles and 80% having more than 5 follicles. (P Value = .901). Regarding the type of infertility, it was found that 13.1% of people suffering from primary infertility had less than 5 follicles, while 86.9% of them were found to have more than 5 follicles. Similar results appeared in the women with secondary infertility, with 27.9% having less than 5 follicles and 72.1% having 5 follicles or more. (P Value= .059). When comparing between the number of follicles and the size of the largest follicle, it was found that the majority of women who had their largest follicle size under 15mm had less than 5 follicles (68.8%), while the rest of them (31.2%) had 5 follicles or more. In contrast, women with their largest follicle size being 15mm or larger had 5 or more follicles (85.7%) more often than having less than 5 follicles (14.3%). (P Value= .000). When comparing the Body Mass Index(BMI) with the number of follicles, women with normal weight had 5 follicles or more (73.7%) more often than having less than 5 follicles (26.3%). Again, similar results were found in women with higher BMI, who are overweight, with 77% having more than 5 follicles and 23% having less than 5 follicles. (P Value= .704)

As Table 3 demonstrates the relationship between certain factors and the results of the pregnancy test. Regarding the age groups, 80.6% of women who were less than 40 years old had a negative pregnancy test, while 19.4% had a positive test. In women who were 40 years old or older, 82.8% had a negative pregnancy test, while 17.2% had a positive test. (P Value= .799). When comparing the types of infertility, 83.1% of women who had primary infertility had a negative pregnancy test, while 16.9% of them had a positive test. In women with secondary infertility, 71.4% had a negative test, while 28.6% had a positive test. (P Value= .163). When comparing the size of the largest follicle found with the results of the pregnancy test, similar results were found with women having negative pregnancy tests in 71.4% and 82.4% in women having largest follicle size of less than 15 mm, and 15 mm or more, respectively. Positive pregnancy tests were found in 28.6% and 17.6% in women with largest follicle size of less than 15mm, and 15mm and larger, respectively. (P Value = .323). Women who had a normal BMI had a negative pregnancy test 89.2% of the time, and positive tests 10.8% of the time. Women found to be overweight had negative pregnancy test 3 times more (75%) than having a positive test(25%). (P Value= .087).

Table 4 shows correlations between certain factors that affect fertility. When correlating the age at the time of collection with the TSH levels, a significant negative correlation (-.201, P Value= .028) was found. Age also correlated positively with the number of follicles. (.221, P Value = .013). The duration of infertility was also found to correlate positively with number of follicles. (.233, P Value= .037), and correlated negatively with size of the largest follicle. (-.244, P Value= .044). Follicular Stimulating Hormone, or FSH, was found to correlate positively with levels of Prolactin (.199, P Value= .029), and negatively correlating with the size of the largest follicle. (-.291, P Value= .001). Estradiol, or E2, was found to correlate positively with number of follicles (.347, P Value= .000), as well as the size of the largest follicle (.333, P Value= .000).

The levels of Prolactin was found to correlate negatively with the size of the largest follicle (-.231, P Value=.010). The total number of follicles was found to positively correlate with size of the largest follicle (.249, P Value=.005). Both Luteinizing Hormone (LH) and the Body Mass Index (BMI) had no significant correlation with any of the other factors that affect infertility.

4. Discussion

We studied many factors that may have an effect on the success rate of assisted reproductive therapy, which showed a few significant predictors of IVF outcomes. A positive pregnancy test was considered a successful IVF. The test was usually done a week or two after the procedure.

Firstly, maternal age correlated positively with the number of follicles (P-value of = 0.013) and duration of infertility (P=.000). In Utrecht University Hospital it was found that women before the age of 37 years showed a mean yearly decline of 4.8%. However, after that age the decline rate was 11.7%.^[2] Meaning as maternal age advances follicular count decreases. This is not the case in this study, were women regardless of their age had more than 5 follicles. However, in this study maternal age did not have a significant correlation with the follicle size. While in a study conducted in Chicago, women under 35 years of age had higher live birth rates and larger mean follicle diameters. In their studied age group the live birth rate per retrieval was 56.5% with mean follicle diameters of 19mm or greater. However, 35.4% of their cases had mean diameters under 19mm.^[3] In addition, it was noted by the results that the duration of infertility affects the number of follicles induced (P=0.037), bearing in mind the correspondence between the total number of oocytes collected from ovaries and IVF success stated in a study by Choe et al. This means that the pregnancy rate increases as the difference between the duration of infertility and number of follicles induced decreases.^[4] Another significant correlation was found between Estrogen levels and the number and size of follicles induced (P=.000) and (P=.000), respectively. This could also be due to the indirect effect of FSH on follicular growth and estrogen biosynthesis^[5] This is possibly the explanation behind the significance found between FSH and the largest follicle (P=.001). Kim I, et al studied the effect of estrogen on follicular development in immature mammals, they found that estrogen significantly increased the number of antral follicles in a guinea pig's ovary, while in rabbit and mice estrogen increased the number of some pre-antral follicles. Hence, it was found that estrogen does not improve follicular maturation in all animal species.^[6] This was also the case in this study, where FSH levels had a negative correlation. Moreover, the effect of FSH on estrogen levels was discussed in a study conducted in Sweden, which stated that FSH alone resulted in an increase in the size of the uterine cavity, polycystic enlargement of the ovaries, and an increase in urinary estrogen output.^[7] Which could explain the reason estrogen levels were also significant with both number and size of follicles. There was also a significant negative correlation noted between the largest follicle's size and duration of infertility.^[3] Which means the longer the infertility period the slighter the chance of IVF success. Furthermore, it is noted in the study that the FSH hormone

levels negatively correlate with the size of the follicle induced. However, FSH levels increase with age, which might mask the effect of age on follicle size and number.^[8] Additionally, Prolactin levels have also shown a negative correlation with the size of the follicles induced. Therefore, the control of prolactin levels might indirectly affect the success rate of IVF.^[9] In a study by Uilenbroek Et Al an inverse relation was found between prolactin and follicular estradiol production in the presence of unchanged serum LH levels, which suggests that prolactin can have a direct action on estrogen biosynthesis of follicle cells. Therefore, it was found that the ability of large follicles to produce estradiol was inhibited by the presence of high serum prolactin levels. This effect might contribute to the reduced fertility seen during hyperprolactinemia.^[9]

5. Conclusion

The fact that IVF treatments have not still reached their anticipated levels of success reinforces the importance of understanding all the factors that may influence the success of IVF. This study aimed to investigate some of these factors and their interaction with one another hoping to reach higher success rates. Although the process of follicular development and the oocyte complex are not as complicated as they were in the past, many aspects remain unknown. This heightens the need for larger controlled studies to analyze how the synchronization of the various factors contributing to infertility lead to a decrease in pregnancy rates.

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Attachments

Table 1: Characteristics of the Sample

Characteristic	Number (Percentage)	Mean Standard Deviation	Minimum	Maximum
Age				
Less than 40 years old	95 (76%)	35.07 (±7.06)	17	49
More than 40 years old	30 (24%)			
Infertility				
Primary	61 (58.7%)	-----	-----	-----
Secondary	43 (41.3%)			
Duration of Infertility	-----	6.98 (±5.01)	1	24
Number of Follicles				
Less than 5 follicles	28 (21.7%)	8.68 (±5.05)	0	29
More than 5 follicles	101 (78.3%)			
Size of Follicles (Largest Follicle)				
Less than 15 millimeters	16 (12.5%)	20.10 (±4.97)	6	40.8
More than 15 millimeters	112 (87.5%)			
BMI				
Normal Weight	38 (38.4%)	27.63 (±5.92)	18.29	41.74
Overweight	61 (61.6%)			
Pregnancy Test				
Positive	23 (18.7%)	-----	-----	-----

Negative	100 (81.3%)			
Hormone Panel				
Estrogen (Estradiol)	-----	3620.55 (±4120.65)	40	27530
Follicular Stimulating Hormone (FSH)	-----	8.89 (±6.58)	1.8	33.4
Luteinizing Hormone (LH)	-----	9.09 (±10.04)	0.02	89.53
Prolactin	-----	436.14 (±513.10)	1	4496
Thyroid Stimulating Hormone (TSH)	-----	3.03 (±2.26)	0.11	19.6

Table 2: Factors Affecting Number of Follicles

Factor	Number of Follicles		P Value
	Less than 5 Follicles	More than 5 Follicles	
Age			
Less than 40 years old	20 (21.1%)	75 (78.9%)	0.901
More than 40 years old	6 (20.0%)	24 (80.0%)	
Infertility			
Primary	8 (13.1%)	53 (86.9%)	0.059
Secondary	12 (27.9%)	31 (72.1%)	
Size of Follicles (Largest Follicle)			
Less than 15 millimeters	11 (68.8%)	5 (31.2%)	0
More than 15 millimeters	16 (14.3%)	96 (85.7%)	
BMI			
Normal Weight	10 (26.3%)	28 (73.7%)	0.704
Overweight	14 (23.0%)	47 (77.0%)	

Table 3: Factors Affecting Success Rate (Positive Pregnancy Test)

Factor	Pregnancy Test		P Value
	Negative	Positive	
Age			
Less than 40 years old	75 (80.6%)	18 (19.4%)	0.799
More than 40 years old	24 (82.8%)	5 (17.2%)	
Infertility			
Primary	49 (83.1%)	10 (16.9%)	0.163
Secondary	30 (71.4%)	12 (28.6%)	
Size of Follicles (Largest Follicle)			
Less than 15 millimeters	10 (71.4%)	4 (28.6%)	0.323
More than 15 millimeters	89 (82.4%)	19 (17.6%)	
BMI			
Normal Weight	33 (89.2%)	4 (10.8%)	0.087
Overweight	45 (75.0%)	15 (25.0%)	

Table 4: Correlations between Fertility Factors

Factors of Fertility	Age at Collection		Duration of Infertility	FSH	LH	E2	TSH	Prolactin	Number of Follicles	Largest follicle	BMI
Age at collection	Pearson Correlation	1	0.452	0.138	-0.127	0.087	-0.201	-0.012	0.221	-0.038	0.193
	P Value		0	0.127	0.167	0.339	0.028	0.896	0.013	0.671	0.056
	Number	125	81	123	120	122	120	122	125	124	99
Duration of Infertility	Pearson Correlation	0.452	1	0.193	0	-0.02	-0.168	-0.097	0.233	-0.224	0.149
	P Value	0		0.089	0.997	0.862	0.138	0.391	0.037	0.044	0.239
	Number	81	81	79	79	79	79	80	81	81	64
FSH	Pearson Correlation	0.138	0.193	1	0.12	-0.052	-0.042	0.199	-0.172	-0.291	0.06
	P Value	0.127	0.089		0.191	0.566	0.65	0.029	0.054	0.001	0.555
	Number	123	79	126	121	123	120	121	126	125	98
LH	Pearson Correlation	-0.127	0	0.12	1	-0.015	0.075	0.029	-0.175	-0.091	-0.142
	P Value	0.167	0.997	0.191		0.872	0.42	0.754	0.053	0.32	0.171
	Number	120	79	121	123	120	119	118	123	122	95
E2	Pearson Correlation	0.087	-0.02	-0.052	-0.015	1	0.123	0.001	0.347	0.333	-0.06
	P Value	0.339	0.862	0.566	0.872		0.183	0.993	0	0	0.555
	Number	122	79	123	120	126	120	120	126	125	98
TSH	Pearson Correlation	-0.201	-0.168	-0.042	0.075	0.123	1	0.109	-0.02	0.025	0.031
	P Value	0.028	0.138	0.65	0.42	0.183		0.241	0.825	0.784	0.765
	Number	120	79	120	119	120	123	118	123	122	97
Prolactin	Pearson Correlation	-0.012	-0.097	0.199	0.029	0.001	0.109	1	-0.053	-0.231	-0.102
	P Value	0.896	0.391	0.029	0.754	0.993	0.241		0.563	0.01	0.317

	Number	122	80	121	118	120	118	123	123	122	98
Number of Follicles	Pearson Correlation	0.221	0.233	-0.172	-0.175	0.347	-0.02	-0.053	1	0.249	0.027
	P Value	0.013	0.037	0.054	0.053	0	0.825	0.563		0.005	0.79
	Number	125	81	126	123	126	123	123	129	128	100
Largest Follicle	Pearson Correlation	-0.038	-0.224	-0.291	-0.091	0.333	0.025	-0.231	0.249	1	-0.136
	P Value	0.671	0.044	0.001	0.32	0	0.784	0.01	0.005		0.179
	Number	124	81	125	122	125	122	122	128	128	100
BMI	Pearson Correlation	0.193	0.149	0.06	-0.142	-0.06	0.031	-0.102	0.027	-0.136	1
	P Value	0.056	0.239	0.555	0.171	0.555	0.765	0.317	0.79	0.179	
	Number	99	64	98	95	98	97	98	100	100	100

