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Infertility Management Outcomes in Correlation to Medical Status

Nareman Elhamamy[1]* and Mohamed Moustafa El Zayat[2]

[1]*Department of Obstetrics and Gynecology, Tanta University, Egypt*

[2]*Department of Engineering and Biotechnology, Royal Fertility Center, Egypt*

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***Corresponding author:** Nareman Elhamamy, Department of Obstetrics and Gynecology, Tanta University, Egypt

Abstract

Background: Research efforts have shown that morbid medical diseases and chronic conditions have common genetic susceptibility aspects to infertility such as cases affected by polycystic ovarian syndrome are shown to have liability for development of type 2 DM.

Aim: To investigate the correlation and linkage between female's disease existing at the time of the ART management cycles and the reproductive clinical outcomes.

Methodology: A retrospective clinical research trial analysis of 1000 IVF and 400 ICSI cycles the research data was obtained from the medical records of cases whether healthy or diseased as regards medical aspects. Cases have undergone the first intended oocyte retrieval cycle all female cases recruited within the research revealed either none or just a single episode of live birth. Live birth involved the birth of at least one living child, irrespective of the gestational duration.

Result: comparative statistical analysis between healthy cases and diseased cases regarding basal laboratory data, oocytes count, sperm count, fertilization rate and outcome in which there was no statistical significant difference basal AMH, FSH, LH, E2,TSH, Oocytes count per patient, Total sperm count (x106/ml), Fertilization rate per patients, (p values=0.093, 0.088, 0.367, 0.132, 0.338, 0.252, 0.739, 0.694 consecutively) however the Rate of clinical pregnancy and cycle cancelation was statistically significantly higher among the health research group(p values= 0.001). Statistical Logistic regression analysis for association between maternal morbid disease and IVF/ICSI outcome among the studied cases in which there was statistical significance as regards clinical pregnancy and cycle cancelation (p values =0.001, 0.003, 0.001, 0.005 consecutively)

Conclusion: The current research study reveal a considerable correlation between most preexisting diseases investigated presenting at the time of the first oocyte retrieval management cycle and lower rates of live birth.

Keywords: Chronic conditions; Reproductive clinical; Gestational duration; Fertilization

Introduction

Research efforts all over the globe have revealed that infertility doesn't take place in a random manner among the population. In an interesting manner it was observed that, infertile cases are categorized by distinct Infertility pathophysiological complex etiologies in some clinical scenarios at molecular and cellular levels [1-5]. Furthermore, the investigators from prior research efforts have revealed that there is clinical, molecular and pathological interactions and linkages between various diseases and infertility as an issue presented in everyday practice. Infertility etiology is considered a part of a large mega disease [6-10].

Clinical diseases causing infertility issues are manifested in various clinical scenarios concomitantly with infertility issues such as DM that is considered one of the serious issues affecting endometrial receptivity in cases requiring ICSI management protocols besides its influence on the immune system making cases affected liable to pelvis inflammatory diseases with its sequala affecting the fertility capacity by tubal blockage [11-13].

Interestingly previous research efforts have shown that morbid medical diseases and chronic conditions have common genetic susceptibility aspects to infertility such as cases affected by polycystic ovarian syndrome are shown to have liability for development of type 2 DM [14,15]. Fertility capacity requires an intact physiological pathway that are affected by different aspects whether at endocrinal diseases, gastrointestinal issues and psychiatric disorders. ovulatory defects are well correlated to different endocrinological issues such as hyper or hypothyroid diseases that denotes that research efforts should focus on investigating the common linkage and origin causing the presenting infertility symptom [16-18].

Aim of the Work

To investigate the correlation and linkage between female's disease existing at the time of the ART management cycles and the reproductive clinical outcomes.

Methodology

A retrospective clinical research trial carried over time from January 2017 till august 2019 in the ART unit of gynecology department on Tanta University teaching hospitals and other private centers for ART included analysis of 1000 IVF and 400 ICSI cycles the research data was obtained from the medical records of cases whether healthy or diseased as regards medical aspects. Cases have undergone the first intended oocyte retrieval cycle all female cases recruited within the research revealed either none or just a single episode of live birth. Live birth involved the birth of at least one living child, irrespective of the gestational duration. All phases of management course from the beginning of controlled ovarian stimulation to the clinical reproductive outcome of the fresh and/or subsequent frozen embryonic transfers have been gathered for data analysis. For this reason, cycles canceled before either oocyte retrieval or embryo transfer were included into the final statistical analysis.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges. Also qualitative data were presented as number and percentages. The comparison between groups with qualitative data was done by using Chi-square test while the comparison between two independent groups with quantitative was done by using Independent t-test. Adjusted and unadjusted logistic regression analysis was used to assess the association between maternal disease and IVF/ICSI outcome. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of < 0.05.

Result

Table1 reveals and displays the Demographic research data, infertility etiology, basal laboratory indices, oocytes, sperm count, incidence and type maternal morbid disease among the investigated cases .in which Maternal age (years) Mean±SD=34.10±2.16 ,Male age (years), mean±SD=34.96±3.44, Maternal BMI (Kg/m2) Mean±SD=22.70±1.50 ,Maternal tobacco smoking, no. (%)=54 (086%) ,Paternal tobacco smoking, no. (%)=833 (59.5%) ,Duration of infertility (years) Mean± SD=2.51 ± 1.55. as regards Infertility etiology, Unexplained=386 (27.57%), Tubal=97 (6.93%), Uterine=181 (12.93%), Endometriosis=70 (5.0%), Ovulatory dysfunction=149 (10.64%) ,Diminished ovarian reserve=133 (9.5%), Multiple female factors, Old age = 30 (2.14%). Concerning Type of menstrual cycle, Regular =1163 (83.1%), Irregular= 225 (16.1%), Amenorrhea=12 (0.86%). Basal AMH (ng/mL), mean±SD=5.07±2.78, Basal FSH (mUI/mL) mean±SD=7.95±3.37, Basal LH (mUI/mL) mean±SD=8.65±4.03 ,Basal E2 (pg/ml) mean±SD=70.59 ± 33.35, Basal TSH (IU/mL)Mean±SD=6.04±2.83, Total number of oocytes retrieved, number Mean±SD=17+/-9 ,Oocytes count per patient, mean±SD=12.37±1.37,Total sperm count (x106/ml), mean±SD=79.99 ± 34.17 ,Fertilization rate per patients, mean±SD=68.02±13.65, Treatment protocol IVF=1000 (71.4%), ICSI=400 (28.6%), as regards Types of morbid conditions, Endocrine, nutritional, and metabolic diseases=198 (50.51%), Diseases of the blood=25 (6.38%), nervous system=22 (5.61%), digestive system=21 (5.36%) , circulatory system=21 (5.36%), respiratory system=20 (5.10%), Mental and behavioral disorders=20 (5.10%), Diseases of the musculoskeletal system=13 (3.32%), Diabetes mellitus=10 (2.55%), Hypertension =9 (2.30%), Other disease=33 (8.42%).

Table 1: Demographic data, infertility etiology, basal laboratory data, oocytes, sperm count, incidence and type maternal morbid disease among the studied.

	Total Number = 1400 Cases
Maternal age (years)	
Mean±SD	34.10±2.16
Range	28 - 39
Male age (years), mean±SD	
Mean±SD	34.96±3.44
Range	29 - 43
Maternal BMI (Kg/m2)	
Mean±SD	22.70±1.50
Range	18.5 - 26.8
Maternal tobacco smoking, no. (%)	54 (086%)
Paternal tobacco smoking, no. (%)	833 (59.5%)
Duration of infertility (years)	
Mean±SD	2.51±1.55
Range	1.2 - 4.2

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Infertility etiology	
Unexplained	386 (27.57%)
Tubal	97 (6.93%)
Uterine	181 (12.93%)
Endometriosis	70 (5.0%)
Ovulatory dysfunction	149 (10.64%)
Diminished ovarian reserve	133 (9.5%)
Multiple female factors	354 (25.29%)
Old age	30 (2.14%)
Type of menstrual cycle	
Regular	1163 (83.1%)
Irregular	225 (16.1%)
Amennorrhea	12 (0.86%)
Basal AMH (ng/mL), mean±SD	
Mean±SD	5.07±2.78
Range	0 - 25
Basal FSH (mUI/mL), mean ± SD	
Mean±SD	7.95±3.37
Range	0.3 - 98
Basal LH (mUI/mL), mean±SD	
Mean±SD	8.65±4.03
Range	0.5 - 127
Basal E2 (pg/ml), mean ± SD	
Mean±SD	70.59±33.35
Range	1.1 - 3033
Basal TSH (IU/mL)	
Mean±SD	6.04±2.83
Range	0.05 – 123
Total number of oocytes retrieved, number	
Mean±SD	17+/-9
Range	0-9
Oocytes count per patient, mean±SD	
Mean±SD	12.37±1.37
Range	7-16
Total sperm count (x106/ml), mean ± SD	
Mean±SD	79.99±34.17
Range	7 - 275
Fertilization rate per patients, mean±SD	
Mean±SD	68.02±13.65
Range	58.4 - 78.9
Treatment	
IVF	1000 (71.4%)
ICSI	400 (28.6%)
Maternal morbid conditions	
Negative	1008 (72.0%)
Positive	392 (28.0%)
Types of morbid conditions	

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Endocrine, nutritional, and metabolic diseases	198 (50.51%)
Diseases of the blood	25 (6.38%)
Diseases of the nervous system	22 (5.61%)
Diseases of the digestive system	21 (5.36%)
Diseases of the circulatory system	21 (5.36%)
Diseases of the respiratory system	20 (5.10%)
Mental and behavioral disorders	20 (5.10%)
Diseases of the musculoskeletal system	13 (3.32%)
Diabetes mellitus	10 (2.55%)
Hypertension	9 (2.30%)
Other disease	33 (8.42%)

Table 2 reveal and display the comparative statistical analysis between healthy cases and diseased cases regarding demographic and clinical characteristics in which Maternal age, BMI ,there was statistically significantly higher among the diseased cases(p values <0.001), statistically significantly difference between both research groups as regards type of menstrual cycle (p value=0.011).however there is no statistical significant difference between research groups (p values=0.102, 0.786, 0.154, 0.111, 0.974, 0.765, 0.512, 0.956, 0.649, 0.418,0.421 ,0.5114 consecutively).

Table 2: Comparison between healthy cases and diseased cases regarding demographic and characteristics.

Parameters	Healthy No. = 1008	Diseased No. = 392	Test Value	P-Value
Maternal age (years), mean±SD	33.27±2.46	34.92±1.86	12.011•	<0.001
Male age (years), mean±SD	34.79±3.56	35.13±3.32	1.635•	0.102
Maternal BMI (Kg/m2)	21.83±1.25	23.56±1.74	20.695•	<0.001
Maternal tobacco smoking, no. (%)	38 (3.77%)	16 (4.08%)	0.074*	0.786
Paternal tobacco smoking, no. (%)	588 (58.3%)	245 (62.5%)	2.033*	0.154
Duration of infertility (years)	2.43±1.62	2.58±1.47	1.595•	0.111
Infertility etiology				
Unexplained	284 (28.17%)	102 (26.02%)	0.001*	0.974
Tubal	70 (6.94%)	27 (6.89%)	0.089*	0.765
Uterine	132 (13.10%)	49 (12.50%)	0.430*	0.512
Endometriosis	48 (4.76%)	22 (5.61%)	0.003*	0.956
Ovulatory dysfunction	107 (10.62%)	42 (10.71%)	0.207*	0.649
Diminished ovarian reserve	98 (9.72%)	35 (8.93%)	0.656*	0.418
Multiple female factors	249 (24.70%)	105 (26.79%)	0.648*	0.421
Old age	20 (1.98%)	10 (2.55%)	0.433*	0.5114
Type of menstrual cycle			8.991*	0.011
Regular	842 (83.5%)	321 (81.9%)		
Irregular	162 (16.1%)	63 (16.1%)		
Amennorrhea	4 (0.4%)	8 (2.04%)		

Bold indicate significant

Data were presented as numbers and percentages or means, standard deviations and ranges

•: Independent t-test; *: Chi-square test

BMI: Body mass index; SD: Standard deviations

Table 3 and Figure 1 reveal and display the comparative statistical analysis between healthy cases and diseased cases regarding basal laboratory data, oocytes count, sperm count, fertilization rate and outcome in which there was no statistical significant difference basal AMH, FSH, LH, E2, TSH, Oocytes count per patient, Total sperm count (x106/ml), Fertilization rate per patients,(p values=0.093, 0.088, 0.367, 0.132, 0.338, 0.252, 0.739, 0.694 consecutively) however the Rate of clinical pregnancy and cycle cancelation was statistically significantly higher among the health research group (p values= 0.001).

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Table 3: Comparison between healthy cases and diseased cases regarding basal laboratory data, oocytes count, sperm count, fertilization rate and outcome.

Parameters	Healthy No. = 1008	Diseased No. = 392	Test Value	P-Value
Basal AMH (ng/mL), mean±SD	4.93±2.82	5.21±2.74	1.681•	0.093
Basal FSH (mUI/mL), mean±SD	8.12±3.32	7.78±3.41	1.707•	0.088
Basal LH (mUI/mL), mean±SD	8.75±3.74	8.54±4.31	0.903•	0.367
Basal E2 (pg/ml), mean±SD	72.19±38.20	68.98±28.49	1.508•	0.132
Basal TSH (mUI/mL)	6.12±2.77	5.96±2.89	0.959•	0.338
Total number of oocytes retrieved, number	12352	4747		
Oocytes count per patient, mean±SD	12.32±1.25	12.41±1.48	1.147•	0.252
Total sperm count (x106/ml), mean±SD	79.65±33.21	80.32±35.13	0.333•	0.739
Fertilization rate per patients, mean±SD	68.17±12.65	67.86±14.65	0.393•	0.694
Rate of clinical pregnancy	333 (33.04%)	94 (23.98%)	10.92*	0.001
Rate of cycle cancelation	185 (18.35%)	103 (26.28%)	10.841*	0.001

Bold indicate significant

Data were presented as numbers and percentages or means, standard deviations and ranges

•: Independent t-test; *: Chi-square test

SD: Standard deviations.

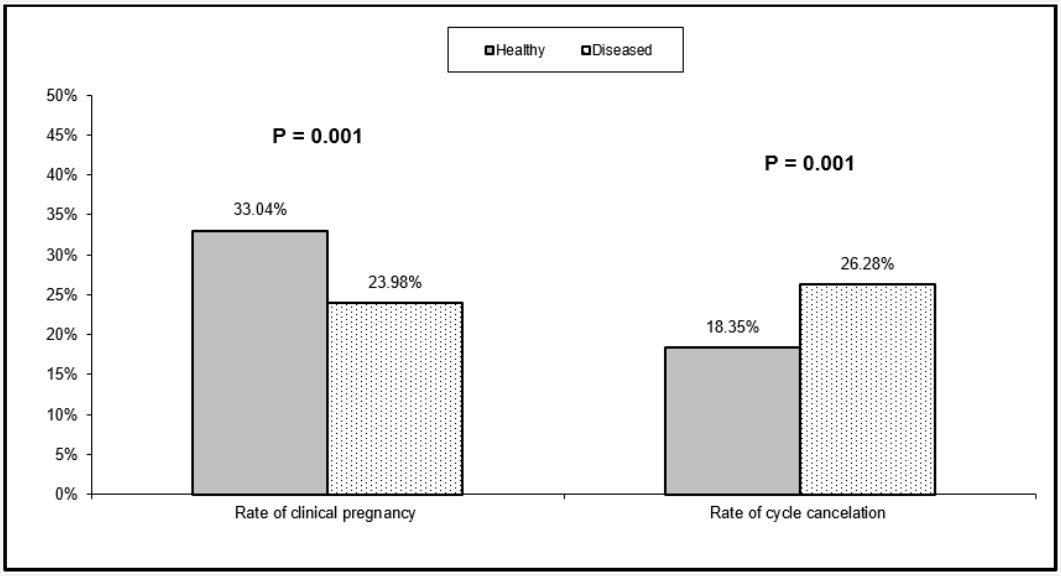

Figure 1: Clinical pregnancy and cancelation rate among healthy and diseased women.

Table 4 statistical Logistic regression analysis for association between maternal morbid disease and IVF/ICSI outcome among the studied cases in which there was statistical significance as regards clinical pregnancy and cycle cancelation (p values =0.001, 0.003, 0.001, 0.005 consecutively).

Table 4: Logistic regression analysis for association between maternal morbid disease and IVF/ICSI outcome among the studied cases.

	OR (95% CI)	P-value	Adjusted OR (95% CI)*	P-Value
Clinical pregnancy	0.6394 (0.4898 to 0.8346)	0.001	0.7135 (0.5136 to 0.8743)	0.003
Cycle cancelation	1.5855 (1.2034 to 2.0889)	0.001	1.6735 (1.3654 to 1.9321)	0.005

OR: Odds ratio; CI: Confidence interval

Bold indicate significant

*: Adjusted for age and BMI of the studied cases

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Discussion

Infertility issues and correlated medical conditions are considered a major challenge to all reproductive specialists and practitioners all over the globe .Co-management of medical diseases and infertility maximizes the cases benefits and upgrades the level of health services offered [2,4,7]. A major research interest is to analyses the correlation and linkage at pathophysiological and clinical levels between various morbid medical diseases and infertility issues and aspects .common molecular and genetic linkages have been demonstrated between infertility issues presenting in every day practice and medical morbid conditions .one of the most famous infertility medical linkages is polycystic ovarian syndrome in which this is considered a metabolic hormonal issue that could present in the form of hirsutism delayed conception or type 2 DM particularly in cases having obesity issues [1,3,8].

Another interesting correlation is cases having psychiatric illnesses taking antipsychotic agents causing hyperprolactinemia. the familial tendency for autoimmune diseases denotes its genetic background and it was well demonstrated that some autoimmune disorders such as systemic lupus have been correlated to infertility aspect such anovulation and reduced endometrial receptivity capacity that was well demonstrated by molecular and genetic bases research efforts [9,11,15].

A previous research effort similar to the current study in approach and methodology have interestingly revealed and displayed the following results in which in comparison and contrast between healthy and diseased females the diseases study subjects have shown lower odds of live birth denoting the lower fertility capacity among medically diseased cases and could be justified by the fact that usually medically affected cases have endocrinal and endometrial issues that hinder the fertility capacity [6,12,14].

Further research data analyses from prior research efforts have revealed an displayed that subclinical iodine-deficiency among hypothyroid cases in conjunction to with autoimmune thyroiditis diseases Had statistically significantly reduced odds of live birth among cases managed by IVF /ICSI Management cycles. [15,18]. Additional research analyses performed by previous investigators have revealed that there is negative impact of medical diseases on odds of cumulative live birth particularly in cases having endocrinal, nutritional, and metabolic illnesses those research findings further verify the current research study findings and could be justified by the fact that impaired physiological aspects in those cases makes the ART management cycles less effective due to defective ovulation and other require fertility tools to maintain gestation that was additionally observed in diabetic cases in previous research efforts being liable to pelvic inflammatory issues causing defective implantation capacity .In an interesting fashion cases having obesity issues had enhanced fertility capacity well demonstrated after bariatric surgeries those findings denote the capability and capacity to upgrade the fertility potential of cases when the proper management line is performed for the chronic morbid condition [5,17].

It was shown in a manner that is in harmony to the current research study data analyses that cases having depressive disorders had non- statistically significant higher odds of cumulative live birth in comparison to healthy women when being on proper medication such as antidepressants that further denotes that medical management of chronic disorders and issues is a part of managing infertility issues presented to the reproductive specialist in every day practice [3,8,18].

Conclusion and Recommendations for Future Research

The current research study reveal a considerable correlation between most preexisting diseases investigated presenting at the time of the first oocyte retrieval management cycle and lower rates of live birth .However future research efforts are recommended to analyze each disease in a detailed manner to infertility issues in an aspect that permits investigating the molecular and genetic issues of both the disease and infertility challenge that permits further verification of the current study results besides would be usefully implemented in future clinical guidelines aiming to upgrade the management protocols of infertility cases.

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