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ORIGINAL ARTICLE

A prospective, cross-sectional study of the protective and risk psychological factors of successful *in vitro* fertilisation outcome: preliminary results in a Greek sample

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ABSTRACT

The aim of this prospective, cross-sectional study was to examine the protective and risk psychological factors associated with the successful outcome of In *vitro* fertilisation (IVF). Various psychological factors that may affect the IVF outcome were measured to a sample of 61 infertile women (mean age 37.2 ± 4.4), who started their first or consecutive IVF treatment cycle in an IVF Unit in Greece. Over half of the participants (50.8%) became pregnant. A binary logistic regression analysis (stepwise) was conducted on pregnancy as the outcome, with various variables as predictors. The model was statistically significant (Omnibus Chi-square $= 27.324$, $df = 5$, $p < .001$), explained 54.7% of the variance, and correctly classified 84.6% of the cases. Life purpose (odds ratio [OR] $= 1.35$, 95% CI $= 1.02–1.78$) and negative emotions (e.g. discontent, sorrow) (OR $= 1.76$, 95% CI $= 1.19–2.60$) were associated with increased pregnancy rates, whereas autonomy (OR $= 0.57$, 95% CI $= 0.39–0.82$), and stress (OR $= 0.69$, 95% CI $= 0.55–0.88$) were associated with decreased pregnancy rates. It has been concluded that the relationship between psychological factors and successful IVF outcome is more complex than commonly believed. The identification of the risk and protective psychological factors could contribute to increased pregnancy rates and foster the implementation of tailored therapeutic interventions.

IMPACT STATEMENT

- **What is already known on this subject?** High levels of infertility stress and/or depression have been associated with lower pregnancy rates. However, little is known on the impact of emotions, personality characteristics and other psychological variables on in vitro fertilisation (IVF) outcome.
- **What the results of this study add?** A combination of commonly believed 'negative' factors (e.g. stress) and 'positive' ones (e.g. well-being) may diversely affect the IVF outcome. Otherwise believed to be positive aspects of human life (i.e. autonomy) may decrease the likelihood of pregnancy, and other factors believed to be 'negative' (e.g. negative emotions) may increase pregnancy rates.
- **What the implications of these findings are for clinical practice and/or further research?** The findings invite researchers to further examine the role of the psychological factors which could potentially affect pregnancy rates. Modifiable factors, such as well-being, stress and emotions, should guide tailored interventions aimed at increasing the pregnancy rates in infertile women.

Introduction

Abundant research evidence suggests that psychological factors may, at least partly, exert an impact upon the outcome of in *vitro* fertilisation (IVF). The studies have mainly focussed on the examination of the role of infertility stress, anxiety and depression (Gürhan et al. 2009) in the success IVF rate. For example, lower levels of baseline depression (Verhaak et al. 2001) and stress (Zhou and Dong 2016) have been shown for the women who became pregnant compared to those who did not. It can be assumed that these factors (depression, stress and anxiety) may minimise the likelihood

of a successful IVF outcome, probably through psychobiological mechanisms.

Based on these findings, psychosocial interventions have been suggested as an indirect way of enhancing successful pregnancy outcomes. A review of the literature suggested that psychotherapy (both group and individual/couple) decreased distress and increased conception rates (de Liz and Strauss 2005). The more recent meta-analysis of 39 studies by Frederiksen et al. (2015) also concluded that psychosocial interventions in infertile couples are effective both in reducing psychological distress and improving pregnancy

rates since women were nearly twice as likely to become pregnant compared to controls.

Scarce evidence also exists on the impact of the expression of emotions on IVF outcome. Women being less expressive of negative emotions before an IVF cycle had lower probability of becoming pregnant and eventually giving birth to a child (De Klerk et al. 2007). A negative association between the expression of negative emotions and IVF success has also been found (Demyttenaere et al. 1998). There is also a paucity of studies investigating the role of personality characteristics (Rockliff et al. 2014) and/or other psychological variables. Taken together, while studies have shown promising results, they are still inconclusive on the effect of the psychosocial factors on pregnancy rates. Little is also known about whether psychosocial positive or protective factors could potentially influence IVF outcome. Positive aspects of well-being (Lowyck et al. 2009), positive affect, life satisfaction and happiness have rarely been investigated and associated with lower distress levels (Rockliff et al. 2014).

In light of this evidence, the psychological factors that could potentially affect the IVF outcome need to be more systematically studied. In most studies, Greek ones included (Gourounti et al. 2011), stress is the only psychological factor assessed. Additionally, stress is assessed during IVF treatment (Wu et al. 2014) and not before starting an IVF cycle. The aim of this study was to examine a number of both protective and risk psychological factors that could potentially be associated with the IVF outcome.

Materials and methods

The unit

The study was carried out at the IVF Unit, Department of Obstetrics and Gynaecology, University of Crete. It covers the geographical area of Crete, which enumerates around 600.000 inhabitants and the workload is about 500–600 cycles per year.

Sample

The inclusion criteria were women, Greeks, aged ≤45, who were entering their first or consecutive treatment cycle of IVF during the study period (January–June 2015). Exclusion criteria were not being Greeks, being illiterate (so not able to respond to the questionnaire items) and being concurrently enrolled in any other study. The final sample included sixty-one infertile women.

Description of the IVF process

Initially, medication was given as a daily injection for about two weeks to suppress the natural menstrual cycle. Following that, follicle stimulating hormone (FSH) was given as a daily injection for about 10–12 days to increase the number of eggs/follicles produced by the ovaries. Regular vaginal ultrasound scans and/or blood tests monitored the ovaries. A trigger hormone injection two to three days before the oocyte retrieval helped the maturation of the eggs. After the egg

retrieval, the fertilisation process followed. The eggs were inseminated with the sperm sample, which was collected on the day of retrieval. Intra-cytoplasmic sperm injection (ICSI) was needed in some cases. The fertilised eggs (embryos) grew in the laboratory from between 2–3 to 5–6 days before being transferred into the uterus (embryo or blastocyst transfer, respectively). During that period, hormone medicines were given to prepare the lining of the uterus to receive the embryo and were continued at least until the pregnancy test and longer once the test was successful. The best one or two embryos were chosen for transfer. After approximately two weeks a blood test showed the results of the IVF cycle.

Measures

The outcome variable was whether the women would become biochemically pregnant or not (as measured with the human chorionic gonadotropin; hCG). A battery of questionnaires was administered to the women at admission to measure the independent variables (i.e. risk and protective factors). Examples of risk psychological factors included perceived stress, couple's negative relating, negative feelings, whereas examples of protective ones included positive feelings, resilience, satisfaction with life, well-being.

The perceived stress scale (PSS) is a 10-item self-report questionnaire that measures how stressful the situations in one's life are considered during the last month on a 5-point scale (0 = never to 4 = very often). An overall score of around 20 is considered moderately high. In this study, the Greek translation (Andreou et al. 2011) was used.

The big five inventory (John and Srivastava 1999) is a 44-item measure of the big five factors (dimensions) of one's personality (i.e. openness, conscientiousness, extraversion, agreeableness and neuroticism) on a 5-point scale ranging from 1 (disagree strongly) to 5 (agree strongly).

The couple's relating to each other questionnaire-3 (CREOQ3) (Kalaitzaki et al. 2016) includes four questionnaires for measuring negative forms of self and other-relating within couples across eight scales (neutral close, upper neutral, lower neutral, neutral distant, upper close, lower close, upper distant and lower distant). In this study, only woman's self-relating towards her partner was used. Items are responded in a 4-point scale (3 = 'Nearly always true', 2 = 'Quite often true', 1 = 'Sometimes true' and 0 = 'Rarely true').

The scale of positive and negative experience (SPANE) (Diener et al. 2009) measures positive and negative feelings during the last month on a 5-point scale ranging from 1 (very rarely or never) to 5 (very often or always). The following scales can be extracted: positive feelings (SPANE-P) by adding the six positive items, negative feelings (SPANE-N) by adding the six negative items and affect balance (SPANE-B) by subtracting the negative feelings score from the positive feelings score, the difference of which can vary from −24 (most unhappy) to 24 (highest affect balance).

The sense of control scale (Lachman and Weaver 1998) is a 12-item scale for measuring the sense of control. For the perceived constraints scale the eight items are scored from

7 = strongly disagree to 1 = strongly agree, whereas for the personal mastery scale the four items are reverse scored.

The resilience scale (RS15) measures the capacity for successful adaptation following adversity. The 15 responses are given on a 7-point scale (1 = strongly disagree to 7 = strongly agree). Summed scores are averaged and range from 1 to 7. In this study, the Greek translation was used (Leontopoulou 2006).

The satisfaction with life scale (SWLS) (Diener et al. 1985) measures one's satisfaction with life on five items. The responses range from 1 ('strongly disagree') to 7 ('strongly agree'). The scores are summed to produce the following ranges: 31–35 (extremely satisfied); 26–30 (satisfied); 21–25 (slightly satisfied); 20 (neutral); 15–19 (slightly dissatisfied); 10–14 (dissatisfied); 5–9 (extremely dissatisfied).

The psychological well-being scale (PWB) (Ryff 1989) is an 18-item measure of six facets of psychological well-being (self-acceptance, environmental mastery, positive relations with others, purpose in life, personal growth and autonomy). The responses range from 1 (totally disagree) to 6 (totally agree).

Six items of the limited disclosure scale (LDS) of the personal and relationships profile (Kalaitzaki 2019) were used to measure the tendency of some participants to be defensive or unwilling to disclose socially undesirable behaviours. Items receive a score from 1 (strongly disagree) to 4 (strongly agree).

Procedure

Women were invited to participate in the study at the intake interview prior to the IVF cycle. Informed consent was assured. Participants completed the questionnaire booklet before starting medication and returned it to the doctor in their ensuing visit. Data were gathered during a six-month period. Both the Research Ethics Committee of the University and the Scientific Committee of the General Hospital where this study took place approved the study.

Statistical analyses

All statistical analyses were conducted with the IBM SPSS 20.0 (Nie et al. 2011). Continuous variables were presented as means ± standard deviation and median (inter-quartile range). Categorical variables were presented as numbers (percentages). Normality of the continuous variables was tested by the Shapiro–Wilks test. The Independent samples t-test or the Mann–Whitney U-test was used as appropriate to compare a number of variables between the women that became pregnant and those that did not according to the parametric test assumptions. The categorical variables were compared by the Chi-square or the Fisher's exact test for 2 × 2 contingency tables (if more than 20% of the expected counts were less than 5; Yates et al. 1999, p. 734). A binary logistic regression analysis (stepwise) was conducted to examine the effects of a number of independent variables (i.e. age, known/or not known infertility cause, stress, personality type, quality of marriage/relationship, positive and negative emotions, sense

of control, psychological resilience, well-being and life satisfaction) on the probability of achieving pregnancy, which was the dependent variable. The results of logistic regression analysis are presented in odds ratios (OR) with a 95% confidence interval (95% CI) (Núñez et al. 2011). A $p < .05$ was considered as statistically significant. Power analysis was conducted using G*Power (Erdfelder et al. 1996).

Results

Of the potential sample of 122 infertile women, 45 were excluded (36.9%) because they were not Greeks and/or they were illiterate (so not able to respond to the questionnaire items). Of the eligible sample, 61 women (response rate: 79.2%) were included in the study. Their mean age was 37.2 years old (±4.4). Most of them had high educational level, were employees in public/private sector, had undergone another cycle prior to the one of the study and the infertility cause was already known (Table 1). The IVF treatment resulted in a high pregnancy rate (50.8%). The demographic and study variables were similar between those who became pregnant and those who did not (Table 1). The exception was that the women who became pregnant were younger than those who did not, had higher levels of neuroticism and lower levels of autonomy. Tendency to avoid revealing socially undesirable behaviours was relatively low ($M = 11.3 \pm 2.4$).

The logistic regression model (Table 2) was statistically significant (Omnibus Chi-square = 22.79, $df = 4$, $p < .001$). The model explained 47.5% (Nagelkerke R^2) of the variance in the dependent variable and correctly classified 76.9% of the cases. It was found (sorted by effect size) that the negative emotions, such as sadness and discontent (odds ratio [OR] = 1.67, 95% CI = 1.16–2.39), and the purpose in life (OR = 1.27, 95% CI = 0.99–1.62) increased the odds of achieving pregnancy. On the other hand, autonomy (OR = 0.63, 95% CI = 0.46–0.85), and perceived stress (OR = 0.73, 95% CI = 0.59–0.91) decreased the odds of achieving pregnancy.

A post-hoc power analysis showed that, with a typical $\alpha = 0.05$ and the commonly recommended $\beta = 0.80$, our sample of $N = 61$ resulted in statistically underpowered findings and an increase in sample size was needed.

Discussion

The aim of this study was to examine whether a number of protective and risk psychological factors could be potentially associated with the IVF outcome. Both protective and risk factors were found to be related to pregnancy rate. This study confirmed the negative impact of stress on the IVF outcome, which is consistent with other studies (Matthiesen et al. 2011; Frederiksen et al. 2015). Furthermore, it was found that one element of well-being (autonomy) decreased the probability of achieving pregnancy. Despite the widespread belief that psychological well-being is a positive aspect of human life (i.e. optimal or most functioning life), it was unexpectedly found that it has a negative impact upon IVF outcome. It can be assumed that women with high

Table 1. Patient demographics for the whole sample compared between pregnant and non-pregnant.

	All	Pregnant ($N = 31$)	Non-pregnant ($N = 30$)	p
Age	37.2 ± 4.4	36.1 ± 4.2	38.4 ± 4.5	.039
Duration of fertility problems (in years)	3.3 ± 2.1	3.5 ± 2.3	3.2 ± 1.9	.594*
First IVF cycle	14 (23.3%)	6 (42.9%)	8 (57.1%)	.327*
Number of IVF	1.7 ± 1.4	2.2 ± 1.4	1.6 ± 1.1	.240*
Known fertility problem	38 (67.9%)	22 (57.9%)	16 (42.1%)	.399
PSS	23.1 ± 6.2	22.5 ± 6.6	23.7 ± 5.9	.467
BFI (extraversion)	26.1 ± 4.5	25.6 ± 3.9	26.5 ± 5.1	.468
BFI (agreeableness)	35.5 ± 6.6	36.1 ± 4.7	34.9 ± 8.3	.847*
BFI (conscientiousness)	34.7 ± 6.1	34.2 ± 6.1	35.3 ± 6.3	.449*
BFI (neuroticism)	25.5 ± 7.4	27.5 ± 7.5	23.4 ± 6.7	.031
BFI (openness)	33.8 ± 8.5	33.4 ± 5.3	34.3 ± 11.0	.667*
SOCS	60.9 ± 10.3	60.2 ± 10.3	61.8 ± 10.6	.543
CREOQ3 (upper neutral)	8.6 ± 5.1	9.1 ± 6.3	8.0 ± 3.2	.813*
CREOQ3 (upper close)	6.7 ± 2.8	6.8 ± 2.7	6.6 ± 3.0	.790
CREOQ3 (neutral close)	5.9 ± 6.4	6.7 ± 8.1	4.9 ± 3.5	.372*
CREOQ3 (lower close)	4.0 ± 2.9	4.3 ± 3.0	3.6 ± 2.8	.416*
CREOQ3 (lower neutral)	8.1 ± 10.3	6.7 ± 2.8	9.5 ± 14.7	.855*
CREOQ3 (lower distant)	6.4 ± 2.9	6.7 ± 3.2	5.9 ± 2.5	.375*
CREOQ3 (neutral distant)	2.2 ± 2.4	2.2 ± 2.1	2.3 ± 2.8	.636*
CREOQ3 (upper distant)	6.8 ± 3.3	7.0 ± 3.7	6.5 ± 2.8	.564
CREOQ3 (Total)	48.5 ± 16.7	49.6 ± 12.7	47.3 ± 20.5	.378*
RS15	85.2 ± 12.1	83.4 ± 11.8	87.1 ± 12.4	.234
SPANE (Total)	38.8 ± 3.0	39.3 ± 2.7	38.2 ± 3.3	.175
SPANE (Positive)	22.0 ± 3.5	21.7 ± 3.0	22.3 ± 3.9	.479
SPANE (Negative)	16.8 ± 4.0	17.6 ± 3.7	15.9 ± 4.3	.102
SWLS	23.2 ± 5.8	22.7 ± 4.9	23.7 ± 6.6	.511
PWB (Positive relations)	17.0 ± 3.4	17.1 ± 3.5	16.9 ± 3.3	.725*
PWB (Self-acceptance)	16.4 ± 3.5	16.3 ± 3.4	16.6 ± 3.6	.623*
PWB (Autonomy)	15.0 ± 3.0	14.1 ± 3.4	16.0 ± 2.2	.014
PWB (Personal growth)	17.1 ± 2.8	16.9 ± 3.1	17.4 ± 2.4	.679*
PWB (Environmental mastery)	15.5 ± 7.3	14.5 ± 3.0	16.6 ± 10.2	.447*
PWB (Purpose in life)	15.1 ± 3.1	15.2 ± 2.8	14.9 ± 3.5	.451
PWB (Total)	96.1 ± 12.4	94.0 ± 10.9	98.3 ± 13.6	.189*
LDS	11.3 ± 2.4	11.8 ± 2.5	10.7 ± 2.3	.085*

Values are presented as mean ± standard deviation and numbers (percentages).
*An asterix indicates a non-parametric test (i.e. Fisher's exact test or Mann–Whitney U).
IVF: in vitro Fertilisation; PSS: perceived stress scale; BFI: big five inventory; SOCS: sense of control scale; CREOQ3: couple's relating to each other questionnaire-3; RS15: Resilience; SPANE: scale of positive and negative experience; SWLS: satisfaction with life scale; PWB: psychological well-being scale; LDS: limited disclosure scale.

Table 2. Regression of psychological factors on pregnancy rates.

	B	S.E.	Wald	Sig.	Exp(B)	OR (95% CI)
Perceived stress	−0.313	0.112	7.785	0.005	0.731	0.587–0.911
Autonomy	−0.470	0.159	8.773	0.003	0.625	0.458–0.853
Purpose in life	0.235	0.127	3.412	0.065	1.265	0.986–1.622
Negative emotions	0.510	0.184	7.684	0.006	1.665	1.161–2.387

autonomy (that is being self-determined and independent) might be oriented towards their personal developments (e.g. career) rather than being particularly motivated to become pregnant.

On the other hand, purpose in life increased the chance of achieving pregnancy. If purpose in life is associated with giving birth to a child, it might be reasonable to assume that it could have a positive effect on pregnancy outcomes, as they might motivate the infertile women to comply with the medical instructions, compromise with the recommendations and all the necessary IVF procedures. However, the mechanism with which this occurs is not yet known, and so further research is needed.

Another unexpected finding was that the negative emotions – and not the positive ones – increased the likelihood of pregnancy. The inability to express emotions (Kakatsaki et al. 2009) and the expression of negative emotions (De Klerk et al. 2007) both have been found to be related with elevated pregnancy rates in women undergoing IVF.

There is abundant literature in psychology indicating that disclosing negative emotions elicits support in close relationships (e.g. Graham et al. 2008) and facilitates stress release. So, expressing negative emotions prior to an IVF cycle might not detrimentally affect the outcome. However, definite conclusions cannot be drawn as the mean scores in this sample were in general low. It might be that high scores have an adverse (detrimental) effect on IVF outcome and this merits further research.

Neuroticism (i.e. vulnerability to stress and negative emotional reactivity) has been positively associated with depression, state and trait anxiety (Rockliff et al. 2014). In this study, it differentiated pregnant from non-pregnant women, but it did not enter logistic regression model. Should the sample size have been larger the results might have been different.

The most important limitations of this study are the limited sample size and the absence of a control group. The high attrition rate restricted the sample significantly, and so did the statistical power and the generalizability of the results. However, a power calculation based on estimates that are likely to be inaccurate (because of a small sample size), may also be inaccurate (Wallace and Melia 2008).

Longitudinal studies examining the predictive validity of several factors, both risk and protective ones, are needed to facilitate the precise and timely identification of women at-risk before an IVF cycle. Factors potentially affecting the

IVF success rate (e.g. body weight, number of retrieved oocytes, AMH level and embryo quality) would have been desirable to be examined between the pregnant and non-pregnant women. Future research should also examine potential mediators, such as coping patterns and social support, which might be equally important to infertility-specific variables in predicting IVF outcome. Future studies need to evaluate the psychological factors in male partners too.

Despite the limitations, to the authors' knowledge, no other study has tried to examine the effects of so many psychological factors concurrently, both risk and protective ones. Most of the studies examine only the effect of stress, particularly during and not before an IVF cycle (Wu et al. 2014), as this study did. Hopefully, a bigger sample will allow more hypotheses to be examined and verify the significance of the present findings. The findings of this study may initiate prevention and intervention efforts to address the modifiable factors, by both extinguishing the risk (e.g. stress) and empowering the protective ones (e.g. well-being, expression of negative feelings). Clinicians may be facilitated to detect infertile women that may be most vulnerable before an IVF cycle and provide them with the necessary guidance and support. It seems that psychological well-being needs to be further studied in order to diversify its potential impact upon successful IVF.

In conclusion, high scores on autonomy and stress were associated with a reduced probability of achieving pregnancy, whereas high scores on negative emotions and purpose in life improved the chances of achieving pregnancy. It seems that the relationship between psychological factors and successful IVF outcome is more complicated than usually believed. It might be a juncture of factors that makes IVF treatment overwhelming. Some factors may pose a negative effect, which might be moderated by the buffering effect of others. So, a number of risk and protective factors in infertile women may diversely affect IVF outcome. The identification of the psychological factors that contribute to increased pregnancy rates will foster the implementation of tailored therapeutic interventions, which along with the medical interventions will hopefully increase the pregnancy rates in infertile couples. Although the findings should be interpreted with caution, they are consistent with the relevant literature and they suggest that there is a potentially promising research area for larger studies to be conducted in the future.

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Disclosure statement

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