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## Role of religion, spirituality, and faith in assisted reproduction

Daniela Paes de Almeida Ferreira Braga<sup>a,b</sup>, Rose Marie Massaro Melamed<sup>a</sup>, Amanda Souza Setti<sup>a,b</sup>, Bianca Ferrarini Zanetti<sup>b</sup> , Rita de Cássia Sávio Figueira<sup>a</sup>, Assumpto Iaconelli, Jr.<sup>a,b</sup> and Edson Borges, Jr.<sup>a,b</sup>

<sup>a</sup>Fertility Medical Group, São Paulo, SP, Brazil; <sup>b</sup>Instituto Sapientiae – Centro de Estudos e Pesquisa em Reprodução Assistida, São Paulo, SP, Brazil

### ABSTRACT

**Purpose:** The purpose of this study is to evaluate the impact of the patient's faith, religion, and spirituality on the outcomes of intracytoplasmic sperm injection (ICSI) cycles.

**Materials and methods:** Eight hundred and seventy-seven patients received a questionnaire containing information on faith, religiosity, and spirituality and the results of the questionnaires were correlated with ICSI outcomes. Patients stated to be Catholic ( $n=476$ ), spiritists ( $n=93$ ), Evangelical ( $n=118$ ), and other religion ( $n=32$ ), and 78 did not identify with any religious group.

**Results:** A significant increase in fertilization, high-quality embryos, and pregnancy rate was found among Spiritists and Evangelicals. Patients who included the infertility diagnosis and treatment in their prayers showed an increased pregnancy rate, and those who reported their faith to be affected by the infertility diagnosis presented a decreased high-quality embryos rate. The high-quality embryos rate was increased among patients who answered that their faith contributed to their decision to undergo infertility treatment. The cycle's cancelation was negatively correlated with the frequency of religious meetings, and the frequency of prayers was positively correlated with the response to ovarian stimulation. Finally, belief in treatment success positively influenced the embryo quality.

**Conclusion:** The findings suggest that spirituality plays a role in adjusting the psychological aspects of an infertile patient.

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Faith; spirituality; assisted reproduction; psychological stress

## Introduction

Worldwide, more than eight in 10 people identify with a religious group [1]. The relationship between religion and medicine has been an extremely controversial topic in several medical areas. The phrase “religion and medicine” is sufficient to trigger strong, not necessarily positive, responses for many people [2]. Religion and spirituality are two common coping techniques people use to address life challenges [3–8], and a growing body of research, from a wide range of disciplines, suggests religion, spirituality, or faith to be an important contributor to health outcomes [7].

Previous published articles have provided evidence of the association between spirituality and well-being [9–12]. Studies have also documented a positive association between religious involvement and better adaptation to medical illness as well as an increased level of well-being and quality of life [4,7,8,13]. Additionally, it has been reported that spirituality and

religion play an important role in the life expectancy of patients with serious diseases [14,15].

It has long been known that patients under significant amounts of stress are more prone to blood pressure elevation, myocardial infarction, stroke, peptic ulcer disease, irritable bowel syndrome, and diseases associated with impaired immune function [7]. If religious involvement helps to reduce psychological stress and increase social support, then it may help to buffer the negative effects of stress on physical health.

Epidemiological evidence suggests that infertility affects approximately 15% of couples at reproductive age [16]. Since the first baby born using *in vitro* fertilization (IVF), assisted reproduction techniques (ART) bring hope for parenthood to thousands of couples considered to be infertile. In recent decades, more than two million children worldwide were born after ART. However, despite recent advances, the number of embryos produced *in vitro* that fail to implant is still high, and more than 50% of couples undergoing ART

cycles do not achieve pregnancy in their first attempt [17–19].

The success of ART depends on numerous biological variables including the cause of fertility, maternal age, protocol for controlled ovarian stimulation (COS), number of retrieved and fertilized oocytes, embryo quality and endometrial receptivity. In addition, considerable evidence suggests that the psychological stress caused by the infertility treatment process also interferes with the success of ART [20–22]. Indeed, it has been demonstrated that both the diagnosis of infertility and the ART treatment are highly stressful [23–25].

Recently, different psychological interventions have been developed with the purpose of minimizing the consequences of an infertility diagnosis and treatment on quality of life. According to Boivin [26], positive results from psychological interventions can be expressed as a decrease in anxiety, tension, worry, fear, and depressive symptoms. For patients diagnosed with infertility, psychological care can affect important parameters, such as reduction of distress, increased adherence to treatment [27], increased confidence in medical procedures [28], change in lifestyle [29], increased knowledge about infertility [30], and improved quality of life [31,32].

If religious and spiritual involvement can reduce psychological stress in people going through serious illness, we have hypothesized that spiritual involvement may positively affect psychological and physical aspects of patients undergoing ART treatments and lead to better outcomes. Therefore, the goal for the present study was to assess the impact of the patient's faith, religion, and spirituality on the outcomes of ART cycles.

## Materials and methods

### Study design

This prospective study included 877 patients undergoing intracytoplasmic sperm injection (ICSI) cycles from April 2016 to June 2017 in a private university-affiliated IVF center. All patients received a questionnaire containing information on faith, religiosity, and spirituality and 797 patients filled the questionnaire while 80 patients did not agree in answering it. The results of the questionnaires were correlated with (i) patient's age, (ii) number of retrieved oocytes, (iii) normal fertilization rate, (iv) number and rate of high-quality embryos, (v) cycle cancelation, (vi) pregnancy cancelation rate, and (vii) pregnancy success. Written informed consent, in which patients agreed to share

the outcomes of their cycles for research purposes, were obtained, and the local institutional review board approved the study.

### Controlled ovarian stimulation and intracytoplasmic sperm injection

Controlled ovarian stimulation was achieved using a daily dose of recombinant FSH (r-FSH, Gonal-F<sup>®</sup>, Merck KGaA, Darmstadt, Germany) beginning on day three of the cycle. Pituitary blockage was performed using a GnRH antagonist (GnRHa, Cetrotide<sup>®</sup>; Merck KGaA, Darmstadt, Germany), and beginning when at least one follicle  $\geq 14$  mm was visualized. When adequate follicular growth and serum E2 levels were observed, recombinant hCG (r-hCG, Ovidrel<sup>®</sup>, Merck KGaA, Darmstadt, Germany), was administered and oocytes were collected after 35 h through transvaginal ultrasound ovum pick-up.

Intracytoplasmic sperm injection was performed according to Palermo et al. (1992). Fertilization was confirmed approximately 16 h after ICSI. Embryos were maintained in a 50  $\mu$ L drop of culture medium (Global<sup>®</sup>, LifeGlobal, Guilford, CT) supplemented with 10% protein supplement covered with paraffin oil in a humidified atmosphere under 6% CO<sub>2</sub> at 37 °C for three to 5 d.

### Embryo morphology evaluation

The embryo morphology was assessed 16–18 h post-ICSI and on the mornings of days two, three, and five using an inverted Nikon Diaphot microscope (Eclipse TE 300; Nikon, Tokyo, Japan) with a Hoffmann modulation contrast system under 400 $\times$  magnification.

High-quality cleavage-stage embryos were defined as those with all of the following characteristics: four cells on day 2 or 8–10 cells on day 3, <10% fragmentation, symmetric blastomeres, the absence of multinucleation, colorless cytoplasm with moderate granulation and no inclusions, the absence of perivitelline space granularity and the absence of zona pellucida (ZP) dysmorphism. Embryos lacking any of these characteristics were considered to be of low quality. Embryo transfer was performed on the third or fifth day of development.

### Clinical follow-up

A pregnancy test was performed 12 d after embryo transfer. All women with a positive test had a transvaginal ultrasound scan after 2 weeks. A clinical

pregnancy was diagnosed when the fetal heartbeat was detected.

### Faith, religiosity, and spirituality questionnaire

All patients filled out a questionnaire before the beginning of the treatment. The questionnaire contained the following questions: (i) What religion are you?, (ii) Do you attend meetings of your religion?, (iii) Do you keep in touch with a leader of your religion?, (iv) Do you pray, if yes, how often?, (v) Do you include the infertility diagnosis and treatment in your prayers, (vi) Has the infertility diagnosis affected your faith?, (vii) At any point has your religiousness negatively affected your decision to go through infertility treatment, (viii) Has your faith contributed to the decision to undergo infertility treatment, (iv) On a scale of 0–10, do you believe in the success of your treatment?.

The answers were compared with the clinical and laboratorial ICSI outcomes.

### Statistical analyses

The effects of (i) patient's religion, (ii) contact with religious leaders, (iii) inclusion of the infertility diagnosis and treatment in prayers, (iv) faith affected by infertility diagnosis, and (v) effect of religiousness on the decision to undergo infertility treatment, on ICSI laboratorial and clinical outcomes were analyzed using Chi-square tests for categorical variables, or ANOVA followed by a Bonferroni *post hoc* test, using age as a covariant, for continuous variables. The results were expressed by mean  $\pm$  standard deviation (SD) or percentage and *p* values. The minimum sample size required considering the effect of patient's religion on ART outcomes (five groups adjusted for age) was 690 subjects, using G\*Power 3.1.7 (SAS Inc., Cary, NC), considering effect size of 15%,  $\alpha$  of 5% and  $\beta$  of 90%.

Linear regression analyses were conducted to study the influence of the frequency of attendance at religious meetings, frequency of prayers and, on a scale of 0–10, how the patient believes in the success of the

treatment, on ICSI outcomes. All regression models were adjusted for patient's age, and the results are expressed as B (linear regression coefficient), confidence interval of 95% (CI 95%) and *p* values. For the linear regression analysis, using effect size of 15%,  $\alpha$  of 5% and  $\beta$  of 90% parameters in G\*Power 3.1.7 (SAS Inc., Cary, NC), the minimum sample size required was 374 individuals.

The statistical analysis was performed on IBM SPSS 20 Software (SPSS Inc., Chicago, IL).

### Results

Among patients answering the questionnaire, 437 reported they were Catholic, 93 reported they were spiritists, 118 were evangelical, 32 had another religion, and 78 did not identify with any religious group. When the effect of the religious group on ICSI outcomes was evaluated, there was a significant increase on fertilization rate, number of high-quality embryos, rate of high-quality embryos, and pregnancy rate that could be seen among patients reporting to be spiritists and evangelical, while Catholics, patients in other alternative religions and those reporting to not have a connection with any religion presented with worse outcomes (Table 1).

No significant difference was noted on ICSI outcomes between patients who reported having contact with leaders of their religions and those who did not. Those who reported that they included the infertility diagnosis and treatment in their prayers presented an increased pregnancy rate, and those who reported their faith to be affected by their infertility diagnosis presented a decreased high-quality embryos rate (Table 2).

When asked if their religiousness had negatively affected the decision to undergo infertility treatment, those who answered yes presented a decreased rate of high-quality embryos. The high-quality embryos rate was, however, increased among patients who answered that their faith contributes to their decision to undergo infertility treatment (Table 2).

**Table 1.** Effect of patient's religion on ICSI outcomes, controlled for patient's age.

Variables	Patient's religion					<i>p</i> -value
	Catholic	Spiritist	Evangelical	Other	No religion	
<i>N</i>	476	93	118	32	78	
Follicles	14.4 $\pm$ 2.1	15.5 $\pm$ 1.7	14.4 $\pm$ 1.6	13.1 $\pm$ 2.1	15.4 $\pm$ 1.8	.496
Oocytes	12.3 $\pm$ 0.4	12.1 $\pm$ 1.3	11.3 $\pm$ 1.4	10.4 $\pm$ 2.6	11.3 $\pm$ 1.3	.398
Mature oocytes	8.3 $\pm$ 0.3	9.2 $\pm$ 1.8	8.1 $\pm$ 0.7	7.3 $\pm$ 1.9	8.7 $\pm$ 1.3	.432
Fertilization rate	82.0 $\pm$ 1.7 <sup>a,d</sup>	89.9 $\pm$ 9.3 <sup>b</sup>	87.0 $\pm$ 3.5 <sup>c</sup>	72.4 $\pm$ 3.7 <sup>d,e</sup>	70.6 $\pm$ 3.5 <sup>e</sup>	<b>.007</b>
High quality embryos number	2.6 $\pm$ 0.2 <sup>a</sup>	3.6 $\pm$ 0.4 <sup>b</sup>	3.0 $\pm$ 0.3 <sup>b,d</sup>	0.9 $\pm$ 1.3 <sup>c</sup>	1.2 $\pm$ 0.6 <sup>c</sup>	<b>.043</b>
High quality embryos rate	32.6 $\pm$ 2.3 <sup>a</sup>	47.1 $\pm$ 3.3 <sup>b</sup>	45.1 $\pm$ 4.3 <sup>b</sup>	36.3 $\pm$ 9.7 <sup>c</sup>	43.1 $\pm$ 5.1 <sup>b</sup>	<b>.063</b>
Pregnancy rate	32.9% <sup>a</sup>	58.0% <sup>b</sup>	33.9% <sup>c</sup>	31.2% <sup>a</sup>	23.0% <sup>d</sup>	<b>.047</b>

Different superscripts in the same line differ.

Bold indicates statistically significant difference with a *p*-value < .005.

**Table 2.** Effect of being in contact with religious leaders, including infertility diagnosis and treatment in their prayers, having had their faith affected by the infertility diagnosis, if religiousness had negatively affected the decision of going through infertility treatment and if their faith had contributed to their decision to undergo infertility treatment on the outcomes of ICSI cycles.

Variables	Contact with religion leader			Including infertility diagnosis and treatment in the prayers			Faith affected by the infertility diagnosis			Decision of going through the treatment negatively affected by the religiousness			Faith contributed to the decision to go through infertility treatment		
	Yes	Not	p	Yes	Not	p	Yes	Not	p	Yes	Not	p	Yes	Not	p
N	326	471		653	144		95	702		12	313		217	106	
Age	37.7 ± 4.7	36.8 ± 3.9	.064	37.1 ± 4.2	37.6 ± 5.1	.358	37.1 ± 3.5	37.1 ± 4.5	.967	38.3 ± 3.0	37.1 ± 4.4	.180	36.9 ± 4.5	37.6 ± 4.2	.186
Follicles	15.8 ± 13.8	15.7 ± 11.0	.945	15.9 ± 12.2	15.2 ± 12.1	.698	14.0 ± 7.8	16.2 ± 12.6	.318	16.2 ± 14.2	15.8 ± 12.1	.906	16.3 ± 12.9	14.9 ± 10.3	.340
Oocytes	10.7 ± 10.6	11.3 ± 8.7	.533	11.2 ± 9.4	10.5 ± 9.7	.579	9.5 ± 6.2	11.4 ± 9.8	.270	7.5 ± 6.8	11.2 ± 9.5	.179	11.0 ± 9.8	11.2 ± 8.7	.847
Mature oocytes	7.8 ± 7.9	8.6 ± 7.2	.346	8.4 ± 7.5	7.5 ± 7.4	.404	7.9 ± 4.7	8.4 ± 7.8	.753	4.5 ± 4.5	8.4 ± 7.5	.079	8.2 ± 7.7	8.4 ± 6.9	.816
Fertilization rate	79.5 ± 22.8	80.4 ± 21.3	.768	80.9 ± 21.5	75.0 ± 21.2	.162	81.2 ± 20.4	79.7 ± 22.3	.725	86.6 ± 35.1	79.9 ± 21.3	.394	81.0 ± 21.7	77.5 ± 22.2	.277
High quality embryos number	2.5 ± 2.4	2.9 ± 2.7	.229	2.7 ± 2.55	2.6 ± 2.5	.795	2.4 ± 2.0	2.8 ± 2.7	.389	1.0 ± 0.0	2.7 ± 2.6	.252	2.8 ± 2.6	2.4 ± 2.7	.301
High quality embryos rate	33.37 ± 30.6	41.3 ± 27.4	.069	38.3 ± 29.5	32.8 ± 24.8	.416	29.9 ± 28.5	39.2 ± 28.1	.050	8.24 ± 11.8	36.8 ± 28.8	.010	38.9 ± 31.1	28.4 ± 21.7	.012
Pregnancy rate	24.2%	29.7%	.390	31.4%	5.5%	.039	18.9%	30.2%	.553	16.6%	28.4%	.464	32.2%	24.5%	.280

Bold indicates statistically significant difference with a *p*-value < .005.

The regression models showed that the cycle's cancellation rate was negatively correlated with the frequency of religious meetings. Moreover, the frequency of prayers was positively correlated with the response to controlled ovarian stimulation, in terms of number of follicles and number of retrieved oocytes (Table 3). In addition, the belief in the treatment's success positively influenced the embryo quality.

## Discussion

It has been reported that faith and spirituality may relieve stress, help the patient to retain a sense of control, and help to maintain hope and a sense of meaning and purpose in life in people with serious illness. Religious involvement appears to enable people, particularly those with serious and disabling medical illnesses, to cope better with their negative health experiences and experience psychological growth, rather than be defeated or overcome by these experiences [14,33].

For the present study, we have hypothesized that if religious and spiritual involvement can reduce psychological stress in people going through serious diseases, then it may positively affect psychological and physical aspects of patients undergoing ART treatments, improving quality of life and the treatment outcome. Therefore, patients undergoing ICSI cycles filled out a questionnaire with information on faith, religiosity, and spirituality and these answers were compared with ICSI outcomes. When asked about their religions, patients who reported they were spiritists presented better fertilization, embryo development and even pregnancy rate when compared with other religions.

The fundamental principle of spiritist theory, or spiritism, is the relation of the material world with spirits. The adherents of the spiritist theory are designated spiritists. According with spiritism, reincarnation, and the survival of the soul after death are vital beliefs. It is stated that through incarnation, lessons are learnt and can be taken into the next life, and every life moves the soul closer to perfection. Reincarnation is a mission, and in order to attain perfection, it is necessary to undergo all the vicissitudes of corporeal existence [34].

It could be argued that the spiritist philosophy can provide powerful tools to help patients cope with their infertility diagnosis and go through the treatment. If fact, the inability to reproduce is an important loss, which may have adverse effects on self-esteem and relationships with others [24,35]. The anxiety and depression associated with infertility are similar to

**Table 3.** Linear regression models of the effect of the frequency of attendance at religious meetings, frequency of prayers and effect of belief in the treatment's success on ICSI outcomes.

Variables	Frequency of meetings of the religion			Frequency of prayers			Belief in the treatment's success		
	B	IC 95%	p	B	IC 95%	p	B	IC 95%	p
Follicles	-0.008	-0.035; 0.020	.581	-0.160	-0.314; -0.007	<b>.041</b>	0.011	-0.002; 0.024	.103
Oocytes	0.009	-0.033; 0.051	.679	-0.227	-0.423; -0.030	<b>.024</b>	0.010	-0.007; 0.026	.243
Mature oocytes	-0.001	-0.045; 0.043	.962	-0.199	-0.450; 0.051	.119	0.010	-0.011; 0.031	.362
Fertilization rate	0.005	-0.015; 0.024	.632	-0.141	-0.474; 0.193	.408	-0.002	-0.010; 0.006	.575
High quality embryos number	-0.098	-0.263; 0.067	.242	0.168	-0.458; 0.794	.597	0.056	-0.011; 0.124	.101
High quality embryos rate	0.004	-0.011; 0.019	.605	0.023	-0.032; 0.078	.416	0.007	0.001; 0.0013	<b>.022</b>
Cancellation rate	-0.726	-1.404; -0.047	<b>.036</b>	1.608	-2.255; 5.471	.413	0.279	-0.045; 0.604	.092
Pregnancy rate	0.668	-0.837; 2.174	.381	2.515	-1.739; 6.769	.244	0.029	-0.564; 0.622	.924

Bold indicates statistically significant difference with a *p*-value < .005.

those associated with other serious medical conditions such as cancer and HIV [36].

Spiritual well-being is significantly associated with less psychological distress [37]. A positive correlation between religious involvement and better adaptation to medical conditions has been reported [38]. This is in agreement with our findings, which suggest that patients who include issues concerning their infertility diagnosis and treatment in their prayers have an increased pregnancy rate. In addition, patients who reported that their faith was affected by their infertility diagnosis, and those who stated that their religiousness have negatively affected their decision to undergo infertility treatment, presented decreased pregnancy and embryo quality rates, respectively. However, embryo quality was increased among patients who answered that their faith contributed to their decision to undergo infertility treatment. This evidence suggests that when faith is weakened, either by the diagnosis of infertility or by the guilt associated with the treatment, the treatment outcome is impaired.

Our results also showed that the cycle's cancellation rate may be affected by the frequency of religious meetings. Moreover, the frequency of prayers may be correlated with the response to controlled ovarian stimulation and finally, belief in the treatment's success positively influenced the embryo quality. These findings suggest that the patient's spirituality contributed to the treatment's success; however, this finding is not yet certain. It could be argued that spirituality helps patients cope with the emotional issues concerning the diagnosis and treatment.

In fact, IVF is psychologically and emotionally stressful. Stress before, during, and/or after the IVF treatment is multidimensional. There is the chronic source of stress caused by the threat of permanent infertility and loss of hope. Another source of stress is the treatment itself, such as daily injections, blood draws, ultrasounds, oocyte retrieval, and the possibility of failure at any of these phases [39]. The influence of

psychological distress on IVF outcome has continued to be the subject of concern, as it has been hypothesized that depression and anxiety may negatively affect hormonal, neuroendocrine, or immunological functioning, thus impairing IVF outcomes [40].

It has previously been demonstrated that a patient's anxiety is associated with both pregnancy rate and live birth rate in IVF patients; the authors suggest that the effect of anxiety may be partly mediated by activities in the hypothalamus-pituitary-adrenal axis (HPA) and sympathetic nervous system [39]. In fact, hypercortisolemia is involved in the dysregulation of HPA axis [41] which in turn may affect the synthesis and release of gonadotrophins. It has also been suggested that norepinephrine and cortisol concentrations may negatively influence the clinical pregnancy rate in IVF treatment [40].

These biological stress markers could be one of the links in the complex relationship between psychosocial stress and outcome after IVF.

According to Pargament [42], psychology primarily helps patients cope with issues that they can control; spirituality or religion primarily helps patients cope with issues that are beyond their control. Spirituality can help people to develop flexibility through experience and positive feelings, to consider the positive aspect of life and the enhancement of hope and satisfaction of life. People who believe in spirituality and use spiritual methods to treat their illness have less pain, suffering, and anxiety [14].

Previous investigations conclude that religious coping may reduce the symptoms of depression. The level of religious commitment also predicts speed of recovery from depression regardless of initial depression severity [4]. Moreover, studies performed in patients with end-stage kidney disease [43,44], AIDS [45], heart disease [46], cancer [14], and other serious medical illnesses [7], also consistently find a high prevalence of religious coping among chronically or seriously ill patients.

Limitations of the present study include ambiguity regarding how prayer, spirituality and faith is understood, duration or types of prayer, or conditions in which prayers, contact with leaders or religious meetings are performed. Further bias may come from the self-report method of data collection, however to the best of our knowledge, the strength of this report is that it is the first to explore the impact of a patient's faith on outcomes of ART and may point the way for new research which might lead to great improvements in therapeutics.

In conclusion, the results presented in this study suggest a relationship between a patient's religion, spirituality and faith on ART outcomes. The reasons behind this relationship have not been thoroughly elucidated to date; however, evidence suggests that spirituality plays a role in adjusting psychological aspects of an infertile patient. Given that prayer or other spiritual approaches are safe and low-risk strategies, ART professionals need to be aware of the use of these strategies as non-pharmacological, noninvasive adjunct therapies.

### Disclosure statement

No potential conflict of interest was reported by the authors.

### ORCID

Bianca Ferrarini Zanetti  <http://orcid.org/0000-0001-7626-3585>

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### ► Current knowledge on this subject

- It has been demonstrated that both the diagnosis of infertility and the infertility treatment are highly stressful. In addition, there is a growing evidence suggesting that religious involvement helps to reduce psychological stress and increase social support, then it may help to buffer the negative effects of stress on physical health.

### ► What this study adds

- There is a relationship between a patient's religion, spirituality and faith on infertility treatment outcomes, therefore assisted reproduction technologies professionals should be aware of the use of these strategies as adjunct therapies.