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CLINICAL ARTICLE

A comparison of psychological stress among women with and without reproductive failure

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ABSTRACT

Objective: To determine whether women with recurrent implantation failure (RIF) after in vitro fertilization (IVF), similar to women with recurrent pregnancy loss, have significantly higher stress levels than women without reproductive failure, and to compare stress levels between women with RIF and women with recurrent pregnancy loss. *Methods:* In a questionnaire-based study between September 2009 and January 2011, psychological stress was measured among patients attending recurrent pregnancy loss and RIF clinics at the Royal Hallamshire Hospital, Sheffield, UK. Participants completed the Fertility Problem Inventory (FPI), the Perceived Stress Scale (PSS), and the Positive and Negative Affect Schedule (PANAS) on their first visit to their respective clinic. Thirty fertile control women also completed the 3 validated questionnaires. *Results:* Compared with the control group, women with RIF and recurrent pregnancy loss had significantly higher scores in the FPI (RIF, $P < 0.001$; recurrent pregnancy loss, $P = 0.003$) and the PANAS negative affect domain (RIF, $P = 0.004$; recurrent pregnancy loss, $P = 0.001$), and lower scores in the PANAS positive affect domain (RIF, $P < 0.001$; recurrent pregnancy loss, $P < 0.001$). Whereas the perceived stress score (PSS) of the recurrent pregnancy loss group was significantly higher than that of the control group ($P = 0.006$), the score of the RIF group was not, although the difference tended toward statistical significance ($P = 0.058$). *Conclusion:* The study findings confirm the stressful nature of RIF and recurrent pregnancy loss.

1. Introduction

Infertility is both a medical and a social problem of global proportions that is often unrecognized in low-income countries, where the focus is primarily on family planning [1]. Infertility in low-resource countries, such as those in Sub-Saharan Africa, may have far-reaching consequences for the affected individuals, including social isolation, economic hardship, and in some cases violence [1].

Involuntary childlessness evokes a stress response that may manifest physically, emotionally, or mentally [2]. Both the diagnosis and treatments for infertility are associated with psychological stress [3]. Women with infertility who fail to conceive with the help of simple treatment options and who require treatment with in vitro fertilization (IVF) may be expected to have developed a high level of stress. The psychological burden of IVF for patients' is well recognized and a cause of premature discontinuation of treatment in many cases [4–7]. A cycle of IVF usually involves the daily injection of fertility medications to stimulate the ovary to produce multiple oocytes, the transvaginal retrieval of these oocytes, fertilization of the oocytes with sperm, and transfer of the embryo to the uterus. Couples then wait up to 2 weeks to find out whether implantation and pregnancy have occurred. This interval between the embryo transfer and pregnancy test has been identified as most stressful [8] Many reproductively challenged women attribute their difficulty in conceiving and failure with assisted conception treatments to psychological stress, but this has not been proven [9].

In a previous study, we evaluated the relationship between stress and recurrent pregnancy loss, one category of reproductive failure [10]. Among women with recurrent implantation failure (RIF)—another category of reproductive failure—the stress level may be further heightened because of uncertainty about the eventual outcome and, for some individuals, the need to make financial compromises and adjustment. The aim of the present study was therefore to determine whether women with RIF, similar to those with recurrent pregnancy loss, have significantly higher stress levels than women without reproductive failure, and also whether women with RIF have different levels of stress compared with women with recurrent pregnancy loss.

2. Materials and methods

In a questionnaire-based study, nulliparous patients newly referred to a dedicated RIF clinic at the Jessop Wing, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, were recruited between September 1, 2009, and January 31, 2011. The study

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was approved by the South Sheffield Research Ethics Committee. All participants were provided with written information about the study and gave written informed consent.

For the purposes of the study, RIF was defined as failure to achieve a clinical pregnancy after the transfer of 4 embryos of good quality in 3 or more fresh or frozen embryo cycles among women younger than 40 years. A good-quality embryo was defined as having the correct number of cells corresponding to the day of its development, and day-5 embryos (blastocysts) were graded in accordance with the expansion and quality of the inner cell mass and trophectoderm [11].

For the comparison of stress levels, nulliparous patients newly referred to a dedicated recurrent pregnancy loss clinic at the Jessop Wing were also included in the study [10]. Recurrent pregnancy loss was defined as 3 or more consecutive spontaneous losses [12]. All patients underwent thorough investigation for the cause of recurrent pregnancy loss according to an established protocol [13]. A diagnosis of unexplained recurrent pregnancy loss was made if the woman fulfilled the criteria of normal parental chromosomal analysis, absence of endocrinologic abnormalities, negative testing for antiphospholipid antibodies and lupus antibodies, normal coagulation, and absence of uterine structural abnormalities [10]. Exclusion criteria for both the RIF and recurrent pregnancy loss groups included a history of psychiatric illness or depression.

For the control group, age-matched healthy fertile women with children and no history of secondary infertility were recruited from the Gynaecology Outpatient Unit at the Jessop Wing. The exclusion criteria for control women included a history of spontaneous pregnancy loss, infertility, pituitary disorders, psychiatric illnesses, and/or depression [10]. All participants in this study were in conjoint relationships.

Psychological stress was measured via 3 validated questionnaires: the Fertility Problem Inventory (FPI), the Perceived Stress Scale (PSS), and the Positive and Negative Affect Schedule (PANAS). Women with RIF and recurrent pregnancy loss completed the questionnaires on their first visit to their respective clinic. The fertile control women similarly completed the 3 validated questionnaires at the Gynaecology Outpatient Unit.

The FPI was developed to measure infertility-related stress. It contains 46 items in 5 psychometric domains that measure social concern, sexual concern, relationship concern, the need for parenthood, and rejection of a childfree lifestyle (Table 1). The instrument uses a 6-point Likert scale (1, strongly disagree; 6, strongly agree). A comprehensive score summed across all questions is used as a global measure of the level of stress. A high score in the FPI indicates a high level of perceived fertility-related stress [14].

The PSS is a widely used psychological instrument for measuring the perception of stress. It is a 10-item self-reported questionnaire and uses a 5-point Likert scale (0, never; 4, very often) [3]. Scores can range from 0 to 40; higher scores indicate a higher level of perceived stress [15].

Table 1
Individual scales in the Fertility Problem Inventory.[a]

Scale	Definition
Social concern	Sensitivity to comments, reminders of infertility, feelings of social isolation, alienation from family or peers
Sexual concern	Diminished sexual enjoyment or sexual self-esteem, scheduled sexual relations difficult
Relationship concern	Difficulty talking about infertility, understanding/accepting sex differences, concerns about impact on relationship
Need for parenthood	Close identification with role of parent, parenthood perceived as primary or essential goal in life.
Rejection of childfree lifestyle	Negative view of childfree lifestyle or status quo, future satisfaction or happiness dependent on having a child (or another child)
Global stress	Total score measuring overall infertility-related stress

[a] Reproduced, with permission, from Ref. [14].

The PANAS contains 20 items that relate to a "positive affect" domain containing 10 items and a "negative affect" domain containing 10 items. A 5-point Likert scale is used for scoring in the PANAS (1, very slightly or not at all; 5, extremely). For both PANAS domains, scores can range from 10 to 50. A higher score in the positive affect domain indicates a greater positive affect (e.g. reflecting happiness), whereas a higher score in the negative affect domain indicates a greater negative affect (e.g. reflecting a depressed or dysphoric state) [16].

Statistical analyses were performed via SPSS version 19 (IBM, Armonk, NY, USA). Mean PSS, FPI, and PANAS scores were compared among the 3 groups of women (RIF, recurrent pregnancy loss, and control) by a 1-way analysis of variance. Mean differences (and their associated 95% confidence intervals) were reported for the 3 pairwise differences (RIF vs recurrent pregnancy loss, RIF vs control, recurrent pregnancy loss vs control). Statistical significance was set at a P value of less than 0.05.

3. Results

During the study period, 27 women with RIF were recruited. The causes of infertility were unexplained (27%), tubal (11%), male factor (26%), endometriosis (14%), anovulation (4%) and 18% had a combination of factors contributing to their subfertility. Thirty-six women with recurrent pregnancy loss were also recruited. The mean number of previous spontaneous losses was 4 (range 3–7) [10]. A total of 30 age-matched healthy fertile women with children and no history of secondary infertility were also recruited.

The mean ± SE age of the women in the RIF, recurrent pregnancy loss, and control groups was 34.7 ± 1.4 years (range 29–39 years), 36.4 ± 0.9 years (range 32–39 years), and 35.5 ± 1.2 years (range 32–38 years). There was no significant difference in age among the 3 groups.

The scores of the psychological questionnaires of the 3 groups are shown in Fig. 1. Compared with the control group, women with RIF and recurrent pregnancy loss had significantly higher scores in the FPI (RIF, $P < 0.001$; recurrent pregnancy loss, $P = 0.003$) and the PANAS negative affect domain (RIF, $P = 0.004$; recurrent pregnancy loss, $P = 0.001$), and lower scores in the PANAS positive affect domain (RIF, $P < 0.001$; recurrent pregnancy loss, $P < 0.001$). Whereas the perceived stress score (PSS) of the recurrent pregnancy loss group was significantly higher than that of the control group ($P = 0.006$), the score of the RIF group was not, although the difference tended toward statistical significance ($P = 0.058$) (Fig. 1). There was no significant difference in stress levels experienced by women with recurrent pregnancy loss and RIF, as measured by the FPI, PSS, PANAS negative affect domain, and the PANAS positive affect domain (Fig. 1).

The various components of the FPI were analyzed separately (Fig. 2). The scores of the recurrent pregnancy loss and RIF groups differed significantly from those of the control women for all components except for relationship concerns referring exclusively to conjoint relationships (Fig. 2).

4. Discussion

The present cross-sectional study has compared stress levels among 3 groups of women. Previous studies have identified infertility, assisted conception treatment, and recurrent pregnancy loss as causes of stress in an individual's life [8,17]; by contrast, the present study has evaluated stress levels among women experiencing RIF after IVF, and compared the results with those of both women experiencing recurrent pregnancy loss and control healthy fertile women. Stress levels were assessed at the first consultation at the RIF and recurrent pregnancy loss clinics via 3 validated questionnaires (PSS, PANAS, FPI). Increased stress scores were found in both the recurrent pregnancy loss and the RIF groups compared with the control group for all 3 validated questionnaires, signifying increased stress levels among these women (Fig. 1). In addition,