# Levels and associations among self-esteem, fertility distress, coping, and reaction to potentially being a genetic carrier in women with diminished ovarian reserve

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**Objective:** To measure the level of distress and its relationship with other psychologic factors in women with diminished ovarian reserve (DOR) who participated in a fragile X genetics study.
**Design:** Longitudinal data analyzed with structural equation modeling.
**Setting:** Four U.S. private and academic fertility centers.
**Patient(s):** Sixty-two infertile patients with DOR.
**Intervention(s):** None.
**Main Outcome Measure(s):** Fertility Problem Inventory, Coping Scale for Infertile Couples, Rosenberg Self-Esteem, Health Orientation Scale.
**Result(s):** Nineteen percent had low fertility distress, 56% had average fertility distress, and 24% had high fertility distress. Thirty-six percent self-reported a "favorable" or "very favorable" emotional response to potentially being a fragile X carrier (termed "emotions"), 53% were "ambivalent," and 11% had an unfavorable reaction. Three months after learning that they were not a carrier, these percentages were 91%, 9%, and 0%, respectively. Emotions at this second time point were significantly more positive than at pretesting. At baseline, higher self-esteem was a significant predictor of reduced fertility distress both directly and indirectly through emotions. Fertility distress was not associated with coping. Self-esteem, fertility distress, pretesting emotions, and coping were unrelated to posttesting emotions.
**Conclusion(s):** The potential of having an explanation for one's DOR condition may have a beneficial impact on women's psychologic states during the process of genetic testing, and this appeared to be especially true for women with higher self-esteem. Psychologic interventions targeted to women with low self-esteem may reduce distress and improve reactions to genetic testing. (Fertil Steril® 2013;99:2037–44. ©2013 by American Society for Reproductive Medicine.)
**Key Words:** Infertility, female infertility, structural equation modeling, diminished ovarian reserve, fragile X, distress, genetic counseling

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Infertility affects ~9% of couples worldwide (1), including ~72 million women aged 20–44 years (1). A reduction in oocyte quantity and quality with advanced age is a normal physiologic occurrence termed "diminished ovarian reserve" (DOR) (2). DOR is diagnosed in ~10% of women seeking fertility assistance (3, 4). Although the average age of female infertility due to normal ovarian aging is the

mid-forties, some women experience DOR much earlier and thus become prematurely infertile. Women with DOR have regular menstrual periods and their diagnosis is generally a surprise because they believe they are fertile if they menstruate regularly (5). These women sometimes project the notion of having "old eggs" onto themselves, resulting in perceptions of the self as being aged and unhealthy (5).

The fragile X mental retardation 1 (FMR1) gene is associated with an increased risk of premature ovarian failure (POF), and the American College of Obstetricians and Gynecologists recommends FMR1 screening in women with elevated FSH before age 40 without known cause (6). FMR1 is a trinucleotide gene measured by the count of cytosine-guanine-guanine (CGG) repeats. An expansion of >200 CGG repeats causes fragile X syndrome, the most common heritable form of mental retardation in male individuals. Male and female individuals with 55–199 CGG repeats are termed "premutation carriers." There is evidence that the premutation carriers (7, 8), and potentially women with high normal (9, 10) or intermediate (8, 11) levels of repeats (35–44 and 45–54 CGG repeats, respectively), have an increased risk of POF and/or DOR.

Involuntary childlessness can cause significant distress for couples, although some adapt well to this stressful life event. Qualitative studies have analyzed the experience of infertility within its social context. Several themes have been described: 1) unanticipated life-course disruption (12, 13); 2) sense of lost time (5, 14); 3) sense of worthlessness, inadequacy, and lack of control (15, 16); 4) social isolation (17); and 5) hope-disappointment cycles (18). In addition to these themes, Dunkel-Schetter and Lobel (19) reported that the following emotional responses to infertility were common according to the literature: grief and depression, anger, guilt, shock/denial, and anxiety. Similar emotional responses have been reported in reaction to a diagnosis of POF (20).

Little is known about the psychologic condition of women with specific infertility diagnoses such as DOR who are facing the prospect of a specific genetic diagnosis. Although publications have formally examined fertility distress in women with infertility diagnoses (21–31), we are unaware of any report examining fertility distress in a preconception genetic testing setting. Other psychologic constructs assessed previously are anxiety, depression, resilience, coping, life events, social support, quality of life, marital adjustment, stigma, disclosure, and overall stress. Pertinent to our study is evidence linking infertility distress with coping (23, 25–27) (although unsupported by others [29]) and self-esteem (32). Mental health has been reported to affect the success of fertility treatment (33, 34).

The purpose of the present report was to examine levels of and hypothesized associations among fertility distress, coping, self-esteem, and emotional reactions to potentially being a fragile X carrier in women diagnosed with DOR. To our knowledge, this is the first report to investigate self-esteem and emotional reactions to potentially being a genetic carrier of a disorder in relation to fertility distress. The specific hypotheses are listed below and illustrated in Supplemental Figure 1 (available online at www.fertstert.org):

- Higher self-esteem is associated with lower fertility distress, as is consistent with related evidence on self-esteem and infertility (19).
- Higher self-esteem predicts a more positive emotional reaction toward potentially being a fragile X premutation carrier. Positive self-views promote adjustment to stressful situations and negative feedback (35, 36). Women's perspective about a potential explanation for their infertility is likely to contribute to the degree of distress they are experiencing. Consequently, having a more positive emotional reaction toward potentially being a fragile X carrier is hypothesized to predict lower fertility distress. Conversely, women who have a more negative emotional reaction to the possibility of being a fragile X carrier are hypothesized to experience greater fertility distress.
- Coping is activated by a greater degree of distress, as is consistent with well accepted stress and coping theories (37).

## MATERIALS AND METHODS

The sample consisted of women diagnosed with DOR who enrolled through reproductive endocrinology and infertility clinics. A description of the underlying study (prevalence study of fragile X trinucleotide repeat levels in women with DOR) appears elsewhere (9). Briefly, eligibility requirements included: diagnosis of DOR (elevated FSH or few antral follicles or low antimüllerian hormone levels), age at DOR diagnosis ≤42 years, and regular menstrual cycles for the preceding 6 months. Criteria for exclusion were: known cause of elevated FSH for one's age unrelated to fragile X (e.g., surgical removal of one or both ovaries, chemotherapy or radiation therapy, Turner syndrome, autoimmune disease), and a family history of fragile X syndrome or premutation.

Participants were enrolled from March 2005 to September 2011 from academic reproductive endocrinology and infertility clinics in California (40%) and North Carolina (19%) and private fertility practices in Virginia (34%) and North Carolina (7%). The study was approved by the Human Ethics Boards at all academic sites (University of Virginia Institutional Review Board no. 11448). Recruitment consisted of targeted mailings, flyers in waiting rooms, and physician referrals. The recruitment methods varied by site and over time.

After providing informed consent, women provided a single blood sample for the genetics analysis (reported previously [9]) and received pretest genetic counseling by a certified genetic counselor. Study materials, biologic samples, and results were deidentified for confidentiality purposes. Psychologic instruments were self-administered at a study visit after the genetic counseling and blood draw. Questionnaires and/or medical record reviews were the source of all demographic, reproductive, and family medical history variables. Follow-up data were obtained by a self-administered questionnaire 3 months after learning the FMR1 test results. None of the participants was a carrier. Of the 62 women in this report with baseline data, 55 (88.7%) completed the follow-up questionnaire. One participant did not want to learn her results and per protocol was not