


Serum Concentrations of Oocyte-Secreted Factors BMP15 and GDF9 During IVF and in Women With Reproductive Pathologies

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Abstract

Oocyte-secreted factors bone morphogenetic protein 15 (BMP15) and growth differentiation factor 9 (GDF9) are critical for folliculogenesis and fertility. This study developed ELISAs for the measurement of BMP15 and GDF9 in serum and investigated their usefulness as biomarkers of female reproductive function. Serum samples were obtained from women undergoing infertility treatments ($n = 154$) and from perimenopausal and postmenopausal women ($n = 28$). Serum concentrations of BMP15 and GDF9 were analyzed in women relative to age, anti-Müllerian hormone, number of oocytes retrieved, and polycystic ovary syndrome (PCOS) after superovulation for *in vitro* fertilization. BMP15 and GDF9 immunoassays were validated for specificity, sensitivity (24 and 26 pg/mL, respectively), and reproducibility. BMP15 and GDF9 were detectable in 61% and 29% of women, respectively. BMP15 and GDF9 varied 64-fold and 15-fold, respectively, between women, but they did not change within subjects following ovarian stimulation with gonadotropins. Serum GDF9 concentration, but not BMP15 concentration, was associated with oocyte number retrieved in patients without PCOS ($P = 0.018$). GDF9 and BMP15 associations with oocyte number differed significantly ($P < 0.05$) with PCOS status. GDF9 concentrations were lower in poor responders (women with fewer than four oocytes retrieved or with cancelled cycles; $P = 0.020$). Serum BMP15, but not GDF9, was lower in women >55 years of age, compared with women of reproductive age ($P < 0.01$). This study develops and validates immunoassays to quantitate BMP15 and GDF9 in human serum and to correlate concentrations with

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serum biomarkers in reproductive medicine.

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