In vitro fertilization in underweight women: focus on obstetric outcome

Cutoff values for abnormal body weight, usually estimated by body mass index (BMI), have been established in medical practice to detect associated metabolic and endocrine alterations responsible for the increased risk of developing a range of health-impairing conditions among underweight and overweight individuals. According to recent statistics by the World Health Organization (1), in developed societies excess body weight (overweight or obesity) constitutes an increasingly common status involving 50%–70% of the adult population. Being underweight is much less common, with a prevalence below 5%, and is thus less of a public health concern, generating significantly less research and publications. In addition, being underweight is frequently secondary to other conditions, such as anorexia nervosa or bulimia, especially in the young population, and as such is often not considered a disease in itself but rather a feature of other diseases that require treatment. This situation is reflected in the field of human reproduction, and especially in assisted reproduction. Many studies clearly state the negative impact of excess body weight on spontaneous and assisted conception, in both men and women (2), but few have focused exclusively on the underweight population and much less in men.

In the context of underweight women it is known that a critical BMI is needed to ensure the correct functioning of the hypothalamic-pituitary-ovarian axis and, therefore, normal ovulation. A 10%–15% reduction in normal body weight is often associated with the cessation of menstrual periods, with anovulation and amenorrhea leading to infertility (3). In fact, a U-shape curve has been described in women with respect to BMI and spontaneous conception, with both extremes of the curve being more related to fertility problems, although more strongly when body weight is excessive.

The use of ovulation induction agents may be enough to provide a solution to infertility in underweight women. This may achieve a correct ovulation and menstruation, as no more implications have been clearly detected for oocyte quality and endometrial receptivity once ovulation is achieved. In fact, underweight recipients of donated ova do not seem to have poorer reproductive outcomes than their normal weight counterparts (4).

However, the greatest concern of underweight women trying to conceive is the plethora of obstetric complications related with a state of undernutrition for mother and fetus, as described in patients with eating disorders. These include an increased risk of hypermesis gravidarum, anemia, impaired weight gain, intrauterine growth retardation, preterm delivery, cesarean delivery, low birthweight, postnatal complications, and postpartum depression (3), and even an increased risk of chronic diseases in the offspring. Therefore, an optimal approach in these women should include adequate preconceptional counseling, regardless of whether conception is achieved naturally, by induction of ovulation, or by in vitro fertilization (IVF). This is especially important when a psychological condition, such as anorexia nervosa or bulimia, or any other chronic disease leading to maternal starvation, has been diagnosed.

The IVF outcome in underweight women has been less studied than in overweight and obese patients. Despite the lack of a clear consensus, it is currently generally considered that results are similar to those in normal weight women, except with regard to obstetric complications, as commented previously. The recent article by Xiong et al. (5) updates and summarizes the available evidence concerning this issue through a meta-analysis of 38 cohort studies with a low risk of bias. The investigators conclude that there are no differences in terms of miscarriage or live birth rates between underweight and normal weight patients, but that clinical pregnancy rates are slightly impaired in underweight women. However, the adjusted odds ratio per cycle level is not significant. Although the unadjusted and adjusted odds ratio per woman level is significant, in their Figure 1 all of the 20 studies included in the analysis of this parameter show a confidence interval crossing or including the unit. In this way, none of the studies independently demonstrated a significant reduction in clinical pregnancy rates in underweight women after IVF; indeed, a modest reduction was evident only when all of them were combined. Because the effect disappeared per cycle level, and miscarriage and live birth rates were similar per cycle or women level, this may have been due to a statistical artifact. As Xiong et al. (5) commented, their findings should be interpreted with caution due to the small number of studies included in the adjusted analyses, the results being potentially underpowered. However, at present, this is the strongest evidence that we have, and it is in line with previous publications.

The message is somehow reassuring—underweight women undergoing IVF present similar results to normal weight women. More and better-designed studies, especially of the randomized type, are desirable to obtain reliable information. Nevertheless, we should not ignore the implications of maternal undernutrition for obstetric and neonatal complications and for the health of the offspring. Thus, the main conclusion to draw from the current medical literature is that adequate preconceptional counseling should be provided to underweight women no matter whether the pregnancy will be spontaneous or assisted, and especially in cases where there are associated psychological or systemic conditions. At present, it seems that, when the nutritional status of the patient is correct, the results for mother and baby are optimal, and being underweight in itself does not seem to impair reproductive outcome after IVF.

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