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Reproductive outcomes in recipients are not associated with oocyte donor body mass index up to 28 kg/m^2: a cohort study of 2722 cycles

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KEY MESSAGE

Obesity has a well-known deleterious effect on reproductive outcomes. No negative effect was observed on the outcomes of oocyte donation cycles with increased donor body mass index (BMI) (up to donor BMI ≤28 kg/m^2). To minimize the negative effect of obesity on these outcomes, this BMI limit should be considered.

A B S T R A C T

The effect of increasing donor body mass index (BMI) on clinical pregnancies was retrospectively analysed in a cohort of consecutive 2722 donor oocyte IVF cycles. The relationship between donor BMI and clinical pregnancies was assessed after adjusting for recipient BMI. Clinical pregnancy rates and live birth rates (LBR) were no different with increasing donor BMI (up to donor BMI ≤28 kg/m^2). The odds of pregnancy did not vary with donor BMI. Compared with donor BMI quartile 1, OR 95% CI of clinical pregnancy was 1.01 (0.82 to 1.25), 1.01 (0.82 to 1.25) and 0.90 (0.73 to 1.12) for quartiles 2, 3 and 4 respectively. A statistically significant reduction of cumulative LBR (P = 0.036) and LBR (P = 0.011) was observed in the results of donation cycles according to recipient BMI quartiles. A reduced odds of clinical pregnancy was observed with increasing recipient BMI. Compared with recipient BMI quartile 1, OR 95% CI of clinical pregnancy was 0.84 (0.68 to 1.03), 0.79 (0.63 to 00.97) and 0.78 (0.63 to 0.971) for quartiles 2, 3 and 4, respectively. A negative effect on oocyte donation cycle outcomes with increased donor BMI was not found after adjusting oocyte donor and recipient BMI.

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Introduction

Overweight and obesity are a global epidemic with a dramatically increasing prevalence over the past 2 decades (Practice Committee of the American Society for Reproductive Medicine, 2015) and with a higher mortality risk from any cause (Clinical guidelines, 1998). They have also been related to negative reproductive results associated with infertility (Awartani et al., 2009; Law et al., 2007; Van der Steeg et al., 2008), subfertility (Bolúmar et al., 2000; Nohr et al., 2009; Wise et al., 2010), a higher risk of miscarriage (Bellver et al., 2003, 2007, 2010; Lashen et al., 2004; Veleva et al., 2008) and complications during pregnancy (Dokras et al., 2006; Koning et al., 2010).

Moreover, an increased body mass index (BMI) is associated with a negative effect on the outcomes of assisted reproductive techniques, with the need for higher doses of gonadotrophins, lower oocyte retrieval and lower fertilization, implantation and pregnancy rates (Luke et al., 2011).

A statistically significant reduction in pregnancy and live birth rates has been observed, as well as an increase in the miscarriage rate in overweight (BMI 25–29.9 kg/m^2) and obese women (BMI ≥30 kg/m^2) undergoing IVF (Rittenberg et al., 2011).

The mechanisms involved in the negative effect of increased BMI on assisted reproduction techniques are unclear. Two mechanisms have been proposed. One would be that obesity affects uterine receptivity owing to a deleterious effect at endometrial level (Bellver et al., 2013); and the other one would be through altered metabolism at ovarian level directly affecting the oocyte (Cardozo et al., 2016).

The oocyte donation model permits the independent analysis of both the effect of BMI on the oocytes (of the donor) and on the endometrial lining (of the recipient).

Bellver et al. (2013) analysed 9578 oocyte donation cycles in which donor BMI was about 21 kg/m^2 and observed a statistically significant reduction in implantation, clinical pregnancy and live birth rates (LBR) in obese recipients (BMI ≥30 kg/m^2), concluding that their study provides clinical evidence of diminished uterine receptivity in these women.

Oocyte quality has been a controversial issue in overweight and obese patients. In a study including 202 oocyte donors (Cardozo et al., 2016), it has recently been suggested that increased BMI in oocyte donors is associated with poorer outcomes in recipient cycles with a reduction in clinical pregnancy rate (CPR). They estimated that a one-unit (1 kg/m^2) increase in BMI is associated with 0.9 times lower odds of achieving a clinical pregnancy (OR 0.9 CI 0.80 to 1.00; P = 0.049).

It would be interesting to be able to confirm the results of previous studies and to ascertain how BMI performs in our population of non-obese oocyte donors. The main objective of this study was to determine the effect of oocyte donor BMI on pregnancy and LBR of the oocyte recipients. As a secondary objective, we analysed the effect of recipient BMI on reception cycle outcomes.

Materials and methods

This is a retrospective observational study of oocyte donation–recipient cycles carried out in the Reproductive Medicine Unit of the Hospital Universitario Dexeus between January 2007 and December 2014.

Inclusion and exclusion criteria

All patients undergoing an assisted reproduction technique with embryo transfer after oocyte donation cycles (fresh plus the subsequent cryopreserved embryo transfers) during the described period were included. The oocyte donors included in our study fulfilled the legal and clinical requirements established by the Spanish regulations on assisted reproduction techniques (RD-Ley, 2014) and our institution-specific inclusion requirements (height >155 cm and BMI 18–28 kg/m^2) (Fernández-Real et al., 2001).

All treated donor cycles in which no embryos were available to transfer owing cancellation for poor response, no retrieval of oocytes or no fertilization, were excluded. The medical records of all our patients include their height and weight within a 6-month period before the ovarian stimulation or endometrial preparation, respectively.

Donor and recipient treatment

The donor screening and stimulation protocols used have been described previously (Barri et al., 2014; Martinez et al., 2006). Briefly, we used a protocol with gonadotrophin releasing hormone (GnRH) antagonist with 0.25 mg of garnirelix (Orgalutran, MSD, Madrid, Spain) combined with 150–200 IU of recombinant FSH (Puregon, MSD, Madrid, Spain). For the final ovulation triggering, a GnRH agonist bolus with 0.2 mg of triptorelin (Decapeptyl, Ipsen Pharma, Barcelona, Spain) was administered when at least three follicles 20 mm or longer in diameter were observed. The oocytes were retrieved 36 h after triggering by means of an ultrasound-guided transvaginal follicular puncture with propofol.

Donors were allocated to recipients according to phenotype, as established by the current Spanish regulations (RD-Ley, 2014). Donors and recipients were synchronized.

Endometrial preparation of the recipients (both for fresh and cryopreserved embryo transfers) was as described by Martinez et al. (2006). Briefly, recipients with normal ovarian function were given an injection of delayed-action GnRH agonist (triptorelin acetate, Decapeptyl 3.75 mg®, Ipsen Pharma, Barcelona, Spain) during the luteal phase (day 20–22 of the cycle). Endometrial priming was achieved with oestradiol valerate, 6 mg/day for 12–15 days (Progynova, Bayer, Barcelona, Spain) plus vaginal micronized progesterone, 600 mg/day (Utrogestan®, Seid, Barcelona, Spain) from the night before oocyte retrieval (day 0). Women with no ovarian function received the same treatment, except for the administration of the GnRH agonist. Plasma oestradiol and progesterone levels were assessed the day before the embryo transfer.

Insemination of donated oocytes was carried out by IVF or intracytoplasmic sperm injection (ICSI) 40 h after HCG administration, according to sperm sample quality. Fertilization was confirmed 16–18 h later. Embryo quality was evaluated according to blastomere number and regularity, degree of fragmentation and the presence of multinucleation. According to the embryo grading system we used, embryos with a score of 8 or over on a scale of 1 to 10 were considered good-quality (Clua et al., 2015).

The remaining embryos were cryopreserved on day 3 or 5 after oocyte retrieval. The slow-freezing method was used until mid-2012 (Solé et al., 2011) and the vitrification method was used thereafter (Cobo et al., 2012).