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This press release is in support of a presentation by Dr Jose Bellver on Wednesday 10 July 2013 at the ESHRE annual meeting in London.

Female obesity linked to lower rates of live birth and embryo implantation in the uterus

Rates decline as BMI increases

London, 9 July 2013: An analysis of almost 10,000 first cycles of egg donation treatment at one of Europe's largest IVF centres shows that female obesity reduces the receptivity of the uterus to embryo implantation and thereby compromises reproductive outcome. The investigators report that excess female weight "impairs human reproduction" and that "the reduction of uterine receptivity is one of the mechanisms involved". As a result they advise weight reduction before pregnancy in any type of conception, including ovum donation.

The study is presented today at the annual meeting of ESHRE by the Spanish gynaecologist Dr Jose Bellver from the Instituto Valenciano de Infertilidad (IVI) in Valencia, Spain.

The effect of excess body weight on female fertility has been widely studied, with most studies finding an adverse effect on outcome. The reasons, however, have been less clearly explained, with effects on cycle regularity and ovulation the most frequently cited.⁽¹⁾ The presence of polycystic ovary syndrome, for example, the most common hormonal reproductive disorder, is regulated in part by body weight.

The study reported today was a review of 9587 egg donation treatments performed at three IVI clinics in Spain between 2000 and 2011. All the egg donors were of normal weight, so their body weight could not confound the results. Egg recipients, however, were of varying body weights, and divided into four groups: lean with BMI below 20 kg/m² (1458 patients, 15.2%),

normal with BMI 20-24.9 kg/m² (5706 patients, 59.5%), overweight with BMI 25-29.9 kg/m² (1770 patients, 18.5%), and obese with BMI \geq 30 kg/m² (653 patients, 6.8%).

When the outcome of the treatment was cross-checked against the BMI of the egg recipient, results showed that the rates of embryo implantation, pregnancy, twin pregnancy and live birth were all significantly reduced as BMI increased.

For example, live birth rate in the four groups was 38.6% in the lean underweight, 37.9% in the normal weight, 34.9% in the overweight, and 27.7% in the obese. Similarly, the rate of embryo implantation in the uterus was 40.4% in the lean underweight, 39.9% in the normal weight, 38.5% in the overweight, and 30.9% in the obese. These trends translated to a statistically significant 27% lower risk of live birth for an obese patient than for one of normal weight (relative risk 0.73).

The investigators acknowledge that there are possible confounding factors in the study (notably that maternal health information was incomplete in the second and third trimesters of pregnancy), but the design of this large study in a series of egg donation treatments ruled out any possibility that the weight of the egg donor (all defined as of normal weight) could affect results in the recipient. The lower level of implantation with increasing BMI suggests an unequivocal effect of recipient BMI.

"Based on our results, the chance of having a baby by egg donation is reduced by around one third for obese women," said Dr Bellver. "More specifically, we found that obese recipients of eggs from normal weight donors had a 23% lower implantation rate than normal weight recipients, 19% lower clinical pregnancy rate, and 27% lower live birth rate."

He explained that, as a systemic disease, obesity "probably affects the different components of the reproductive system independently". For example, some common pathophysiological pathways, such as hyperandrogenism or insulin resistance, may be involved. In the ovary, menstrual irregularity and infertility have been described in women with weight excess. "However," said Dr Bellver, "even in obese ovulatory women conception rates are reduced, showing that ovulation is not the only mechanism underlying this poor outcome. Oocyte and embryo quality also seem to be affected, although it is not known exactly how yet." Results of

this study now suggest impaired endometrial receptivity may also contribute to the decline in fertility in obese women.

"The clinical evidence is now strong enough for implementing preconceptional health policies for obese patients considering assisted reproduction," said Dr Bellver. The control of excess weight, especially through lifestyle interventions, should be mandatory not only for improving reproductive and obstetric outcomes, but also for reducing costs derived from the greater consumption of drugs in IVF, failed treatments, maternal and neonatal complications, and metabolic and non-metabolic diseases in the offspring."

Abstract 175, Wednesday 10 July, 14.00 BST

Obesity and impaired uterine receptivity: clinical experience from 9,587 first cycles of ovum donation

Notes

1. Several studies have shown that female obesity reduces the live birth rate in IVF and increases the risk of miscarriage. The evidence is considered so strong in some countries (or by some clinics) that occasionally strict restrictions exist for access to fertility treatment by obese women. An explanation for the association is not fully understood, but most studies implicate an adverse effect on ovarian function and oocyte quality, with added complications from age and polycystic ovary syndrome.

* When obtaining outside comment, journalists are requested to ensure that their contacts are aware of the embargo on this release.

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