Perinatal complications of oocyte donation to women of advanced reproductive age

More than 23 years have passed since the initial report of pregnancies after oocyte donation in women over the age of 50 (1). Since that time, the Ethics Committee of the American Society for Reproductive Medicine has twice addressed the issue of oocyte or embryo donation to women over the age of 50. In the more recent committee opinion (2), the committee reviewed the available data and concluded that "some women over the age of 50, particularly in the age range of 50–54, who are healthy and well-prepared for parenting, are candidates to receive donated eggs." Whereas pregnancies in this age group are still relatively uncommon, they are not rare. More than 300 births take place annually in women over the age of 50 as a result of fertility treatment in clinics that report to the Society for Assisted Reproductive Technology (3).

In spite of these numbers, only a small number of series reports have addressed the question of perinatal outcomes and obstetric complications. This is likely due to the difficulty of gathering a sufficiently large number of cases in any one institution. Counseling prospective recipients of oocyte donation in this age group has thus been based on limited data, and there remain many unanswered questions. How much additional risk is experienced by women conceiving at age 50 as opposed to age 45? Are the risks to mother and baby in women over 50 years old sufficiently high that these patients should be offered the option of gestational surrogacy?

In the current issue of *Fertility and Sterility*, Guesdon et al. (4) present the experience of a single obstetric unit in France with deliveries after oocyte donation in women over the age of 45. The analyses of 40 deliveries in women over 50 years and 146 deliveries in women between 45 and 49 years add to our understanding of the outcomes of these pregnancies. Furthermore, because all deliveries took place in one obstetric unit, there was likely to be greater similarity in the obstetric management among the cases, thus allowing a sharper delineation of the effect of age in this older group. Would this internal consistency help demonstrate the risks posed by conception after the age of natural menopause?

It is interesting that the complication rates were very similar between the women aged 45 to 49 and those aged over 50. Consistent with prior reports, the overall pregnancy outcomes were very good, in spite of a multiple gestation rate of 35%. There were no maternal deaths. Postpartum hemorrhage resulted in an unusually high number of emergency hysterectomies (four), but the investigators noted that the patients' advanced age may have influenced the obstetric decision to perform a hysterectomy rather than a more conservative procedure.

A relatively high rate of obstetric complications was observed in the group as a whole, but few differences were noted between the two age groups. The rate for preeclampsia, for example, was 20% for women aged between 45 and 49, with a statistically similar rate of 24% for those over age 50. Previous series of pregnancies resulting from oocyte donation in this age group, and even in women in their early 40s, have reported rates for preeclampsia of 20% to 35%, which is consistent with the observations in the present report. The only statistically significant differences between the two age groups was the higher rate of fetal growth restriction in singletons in women over 50 years and the rate of pregnancy-related hypertension in singletons in the older group.

The investigators specifically looked at twin gestations, and again they found no statistically significant differences between outcomes in the two age groups. However, as expected, the twin gestations had a substantially higher rate of complications than the singleton pregnancies, with higher rates of preterm premature rupture of membranes, lower birth weights, and deliveries at an earlier gestational age. Because the series came from an obstetric unit, the investigators were able to report antenatal hospitalization rates; these were similar for the younger and older groups, and were 69% for twin gestations for the group as a whole. Even the women with singleton pregnancies had a 26% risk of an inpatient stay before delivery. There was no difference in the incidence of admissions to the neonatal intensive care unit between the singleton and twin pregnancies, although the duration of neonatal intensive care unit hospitalization was not reported.

What can we conclude on the basis of this and previous reports? Overall, the data are reassuring that with modern obstetric management the large majority of pregnancies in older women can be managed with good outcomes. It is still not clear whether there is a "threshold" age beyond which there is a dramatic increase in complications, as there were few differences noted in this study between the women aged 45 to 49 and those over 50. Because all these pregnancies are necessarily the result of oocyte donation, the additional effect of donated gametes on the incidence of preeclampsia may enhance or even overshadow the effect of age. It is also still unclear whether there is a physiologic limit for recipient age. Only one previous study (5) looked specifically at women aged 55 or older and found a 60% incidence of preeclampsia, but there were only 10 women in that subgroup.

Because there are no other series in women over 55 years old, it seems reasonable that this group should be approached with caution. It is still unclear what preexisting medical conditions should be considered contraindications to pregnancy in women over 45 years. Most practitioners avoid treating women with chronic hypertension because of the already high incidence of pregnancy-related hypertensive disorders in the older age group.

What we do know in 2016 is that in women over 45 years old pregnancies are more complicated than those of younger women, and that prospective recipients of oocyte donation should be counseled about the high rate of antenatal hospitalization. Above all, they should be counseled about choosing single-embryo transfer to minimize the mostly avoidable risk of multiple gestation.

Richard J. Paulson, M.D.
USC Fertility, Keck School of Medicine, University of Southern California, Los Angeles, California

http://dx.doi.org/10.1016/j.fertnstert.2016.10.019

You can discuss this article with its authors and with other ASRM members at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/12663-23222

REFERENCES

1. Sauer MV, Paulson RJ, Lobo RA. Pregnancy after 50: application of oocyte donation to women after natural menopause. Lancet 1993;341:321–3.
2. Ethics Committee of the American Society for Reproductive Medicine. Oocyte or embryo donation to women of advanced age: a committee opinion. Fertil Steril 2013;100:337–400.
3. Yeh JS, Steward RG, Dude AM, Shah AA, Goldfarb JM, Muasher SJ. Pregnancy outcomes decline in recipients over age 44: an analysis of 27,959 fresh donor oocyte in vitro fertilization cycles from the Society for Assisted Reproductive Technology. Fertil Steril 2014;101:1331–6.
4. Guesdon E, Vincent-Rohfritsch A, Bydlowski S, Santulli P, Goffinet F, Le Ray C . Oocyte donation recipients of very advanced age: perinatal complications for singletons and twins. Fertil Steril 2017;107:89–96.
5. Paulson RJ, Boostanfar R, Saadat P, Mor E, Tourgeman DE, Slater CC, et al. Pregnancy in the sixth decade of life: obstetric outcomes in women of advanced reproductive age. JAMA 2002;288:2320–3.