Pregnancy and child outcome after oocyte donation

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During the last decade oocyte donation has been highly successful for treating women previously thought to be hopelessly infertile. The pregnancy rate after oocyte donation is among the highest reported for any fertility-enhancing procedure. Most investigators have noted an increased rate of obstetric complications in these pregnancies. In particular, pregnancy-induced hypertension appears to occur more often than expected, and the Cæsarean section rate is high. However, the majority of oocyte recipients experience a favourable pregnancy and perinatal outcome. When perinatal complications occur they are usually related to multiple gestation. The high frequency of multiple pregnancy after oocyte donation, as well as in all other fields of assisted reproduction, deserves attention, and efforts to avoid multi-fetal gestation must be made. There are only a few studies on post-natal growth and development of young children born after oocyte donation. The health of these children appears to be within normal ranges. The psychological consequences of the treatment on the child require further investigation. Thus far, studies have shown normal socio-emotional development in the child and a warm relationship between the parents and the child in oocyte donation families.

Key words: complications/infertility/oocyte donation/post-natal development/pregnancy

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Introduction

The desire to have children is an inborn human characteristic. Various methods of assisted reproduction have helped thousands of involuntarily infertile couples to fulfil their dreams of having offspring. One of these methods is donation of oocytes from one woman to another. When originally introduced in 1984 (Lutjen et al., 1984), this technique allowed women without ovarian function the opportunity to experience biological parenthood. Since then, the indications for oocyte donation (OD) have evolved to include repeated failed attempts in earlier IVF, inheritable diseases, and advanced age of the woman. At present, OD is practised in at least 14 European countries (Schenker et al., 1997). Thousands of OD have been carried out all over the world and this method has established itself as a standard and most rewarding alternative in family building.

In recent years, there has been growing interest in the outcome of pregnancies resulting from assisted reproduction techniques. Questions have been raised regarding issues such as whether there is any association between the type of conception and the obstetric and perinatal outcome. What are the risks for the offspring? What do we know about the post-natal health and development of children born? Several authors have investigated the outcome after standard IVF (Doyle et al., 1992; Tanbo et al., 1995), after intracytoplasmic sperm injection (ICSI) (Bonduelle et al., 1996; Wennerholm et al., 1996), and after replacement with cryopreserved embryos (Bonduelle et al., 1996; Wennerholm et al., 1997). It seems that the main problem of IVF is the high rate of multiple pregnancies, leading to paediatric complications and a subsequently high rate of perinatal adverse outcome. However, singleton pregnancies achieved after standard IVF also appear to bear an increased risk of prematurity and low birthweight (Tarlatzis and Grimbizis, 1999). This may be related to the cause of infertility, advanced maternal age or a high degree of primiparity. Later on, growth and development of IVF and ICSI children, as well as children born after cryopreservation appear to be within normal ranges.

OD represents a special case in the treatment of infertility in many ways. The pregnancy is unique, as it is achieved from an embryo that is immunologically foreign to the mother. The method involves a third party, the oocyte donor, which makes the treatment ethically and psychologically much more complicated than conventional IVF. Oocyte recipients often differ from traditional IVF patients as regards the cause of infertility and medical history. As OD has extended to include women at a relatively advanced age, it has also brought increased medical and obstetric risks, which may be reflected in the wellbeing of the
child in the future. However, only a very few publications deal with the management and outcome of these pregnancies. Even more limited is information regarding the long-term growth and development of these children.

**Obstetric outcome**

Thus far, most investigators have observed an increased risk of obstetric complications in OD pregnancies (Table I). The frequency of vaginal bleeding during the first trimester is 12–53% (Pados et al., 1994; Abdalla et al., 1998; Söderström-Anttila et al., 1998). Pregnancy-induced hypertension (PIH) occurs at an incidence of 16–40% of oocyte recipients, and the Caesarean section rate is high, 40–76% (Serhal and Craft, 1989; Blanchette, 1993; Pados et al., 1994; Sauer et al., 1996; Abdalla et al., 1998; Söderström-Anttila et al., 1998; Yaron et al., 1998; Salha et al., 1999). Sauer et al. (1996) reported antenatal complications in 38% of a group of oocyte recipients whose mean age was 47 years. Recipients with ovarian failure appear to have a higher incidence of complications, such as first trimester bleeding and pre-eclampsia, than women with functioning ovaries.

The reasons for the increased occurrence of complications in OD pregnancies are unclear. Possible explanations are a high rate of primiparity, multiple pregnancies, and advanced maternal age.

**Table I. Obstetric outcome in oocyte donation pregnancies. Values in parentheses are percentages**

<table>
<thead>
<tr>
<th>Authors</th>
<th>No of pregnancies</th>
<th>First trimester bleeding</th>
<th>Pregnancy-induced hypertension</th>
<th>Caesarean section</th>
<th>Postpartum haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdalla et al. (1998)</td>
<td>140</td>
<td>17 (12)</td>
<td>32 (23)</td>
<td>96 (69)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>Blanchette (1993)</td>
<td>5</td>
<td>2 (40)</td>
<td>2 (40)</td>
<td></td>
<td>2 (40)</td>
</tr>
<tr>
<td>Pados et al. (1994)</td>
<td>52</td>
<td>18 (35)</td>
<td>17 (33)</td>
<td>33 (64)</td>
<td></td>
</tr>
<tr>
<td>Sauer et al. (1996)</td>
<td>74</td>
<td>12 (16)</td>
<td>48 (65)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serhal and Craft (1989)</td>
<td>21</td>
<td>8 (38)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Söderström-Anttila et al. (1998)</td>
<td>51</td>
<td>27 (53)</td>
<td>16 (31)</td>
<td>29 (57)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Yaron et al. (1998)</td>
<td>155</td>
<td>24 (16)</td>
<td>118 (76)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table II. Perinatal outcome in oocyte donation pregnancies**

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of deliveries</th>
<th>Mean birth weight (g)</th>
<th>No of infants with birth weight &lt;2500g (%)</th>
<th>No of preterm deliveries &lt;37weeks (%)a</th>
<th>No of multiple pregnancies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdalla et al. (1998)</td>
<td>total 140</td>
<td>35 (25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>singleton 105</td>
<td>30 (25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>twins 32</td>
<td>33 (52)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>triplets 3</td>
<td>9 (100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Applegarth et al. (1995)</td>
<td>total 49</td>
<td>30 (60)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>singleton 30</td>
<td>3183</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>multiple 19</td>
<td>2286</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pados et al. (1994)</td>
<td>total 52</td>
<td>1 (2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>singleton 44</td>
<td>3218</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>twins 8</td>
<td>2558</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sauer et al. (1996)</td>
<td>total 74</td>
<td>9 (12)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>singleton 45</td>
<td>3218</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td>twins 24</td>
<td>2558</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>triplets 5</td>
<td>1775</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Söderström-Anttila et al. (1998)</td>
<td>total (live born)</td>
<td>49 (25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>singleton 39</td>
<td>3338</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>multiple 10</td>
<td>2216</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yaron et al. (1998)</td>
<td>total 155</td>
<td>10 (50)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>singleton 104</td>
<td>3022</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>twins 43</td>
<td>2291</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>triplets 8</td>
<td>2079</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

aAs a percentage of number of deliveries.
bCalculated from papers with exact data mentioned.
However, immunological factors may play an important role in the development of pre-eclampsia and one proposed theory is that there is inadequate immunoprotection of the fetus–placental unit in oocyte recipients (Serhal and Craft, 1989). The fact that these pregnancies appear to bear increased risks underscores the importance of careful and adequate patient selection before treatment. This is especially important as regards women with some particular medical disorders, or advanced age. The incidence of many diseases, e.g. hypertension, heart disease, diabetes mellitus, and cancer increases as women grow older. With advancing age, obstetric complications occur with increasing frequency regardless of whether conception is spontaneous or assisted (Berkowitz et al., 1990; Cnattingius et al., 1992). OD pregnancies should be considered high-risk pregnancies even in young recipients (Pados et al., 1994; Abdalla et al., 1998; Söderström-Anttila et al., 1998). These facts make it evident that thorough medical screening is particularly critical as regards successful outcome among recipients aged 40–50 years (Sauer et al., 1996). Although there are reports of favourable pregnancy outcome in women aged >50 years (Antinori et al., 1993; Sauer et al., 1993), experience is limited and, even though extensive medical screening does appear to prevent obstetric complications, OD treatment of post-menopausal women should be avoided. Women with Turner’s syndrome have a high risk of cardiological abnormalities, and aortic dissection has been reported during pregnancy in two women with Turner’s syndrome (Nagel and Tesch, 1997). These patients should undergo cardiological assessment, including echocardiography, before treatment. However, pregnancy outcome among recipients with Turner’s syndrome is usually favourable (Foudila et al., 1999).

### Perinatal outcome

Reports on neonatal characteristics of infants born after OD are few (Table II). The mean birthweight of infants was 3000–3400 g in singleton pregnancies and 2300–2500 g for twins (Pados et al., 1994; Applegarth et al., 1995; Sauer et al., 1996; Yaron et al., 1999). In a group of mothers aged >45 years, neonatal complications occurred in 5%, but there were no maternal or neonatal deaths (Sauer et al., 1996). Most centres have reported a perinatal mortality rate of 0–3%. In the literature there are very few reports of congenital malformations in OD infants and it appears that this risk does not differ from that expected in the general population. Recently, we presented the results of a study on the neonatal outcome of a total cohort of 61 OD infants conceived at our clinic between 1992 and 1996, including two still births (Söderström-Anttila et al., 1998). One third of the infants developed from cryopreserved embryos. The outcome was compared with that of a control group of 126 IVF infants. We found no differences in birthweight, incidence of prematurity and intra-uterine growth retardation (IUGR) between these two groups of infants. In the OD group, 13% of the singleton and 30% of the multiple births (two sets of triplets included) were preterm. The incidence of low birthweight (<2500 g) was 10% among OD singletons and 38% among OD twins. The frequency of IUGR was 5% in the OD singleton group and 40% in the OD multiple group. One major malformation (sternum cleft) and one minor malformation (small dermoid cyst) occurred in two OD infants. One third (36%) of the singleton OD infants were still in hospital at the age of 1 week, compared with only 13% of the IVF singletons (P < 0.01). This was at least partly due to the mother of the child, as there was a much higher Caesarean section rate among OD recipients than among IVF mothers.

In an extensive study on obstetric outcome of 232 OD pregnancies, a higher risk of IUGR infants in recipients with ovarian failure was observed (Abdalla et al., 1998) than in women with functioning ovaries. The overall incidence of preterm infants was 13% among singletons, 56% among twins and 100% among triplets, the frequency of birthweight <2500 g was 18% (singletons), 52% (twins) and 100% (triplets), and the frequency of IUGR infants was 15% (singleton), 31% (twins) and 78% (triplets). In fact, in all studies published on OD outcome, a huge increase in neonatal complications in relation to multiple gestation has been found. This is in accordance with findings from standard IVF pregnancies (Bergh et al., 1999). To avoid prematurity, low birthweight and IUGR among the offspring we must stop transferring more than two embryos at a time and even consider replacement of only one embryo. There is excellent experience with this type of approach in an IVF programme (Vilksa et al., 1999). The pregnancy rates with donated oocytes are among the highest reported for any fertility-enhancing procedure, including conventional IVF. We have also learned that the outcome of OD is highly dependent on the age of the donor (Cohen et al., 1999). Especially if the donor is young, the embryo quality is good and the recipient woman already has increased obstetric risks, elective transfer of only one embryo at a time should definitely be considered in OD programmes.

### Health and growth of OD children

To date, only a few studies have specifically addressed follow-up of the health and development of children born after OD. A small group of 14 children born after singleton OD pregnancies was examined (Raoul-Duval et al., 1992, 1994). Follow-up at the ages of 9 months, 18 months and 3 years included a questionnaire on child development covering diseases and functional disorders. The information obtained was correlated with the mother’s emotional state. The psychomotor development of the OD children was found to be normal and the mother–infant relationship was harmonious in every case.

In a questionnaire survey of 51 children aged 12 weeks to 7 years and conceived by OD, all were reported to enjoy good health and normal development in spite of some initial health problems (Applegarth et al., 1995).

We carried out a questionnaire study of post-natal health and development of the total cohort of OD children conceived in our centre between 1992 and 1996 and representing 59 children (39 singleton; 20 multiples) at the age of 0.5 and 4 years (Söderström-Anttila et al., 1998). Information was received from all parents. The results were compared with those from a control group of 126 IVF children. At the time of the study all OD children were healthy. No cases of hearing, visual or neurological defects were reported. All but one of the 59 OD children showed normal height, weight and head circumference development. Surgical intervention had been carried out in 8% of the OD children and 13% of the IVF children. Walking and talking achievements were normal.
Eating and sleeping disorders were uncommon in both groups of children. The IVF mothers were more concerned about certain aspects of the child’s behaviour than the OD mothers. The OD parents observed less fear of strangers in their children compared with the IVF group. The findings in the OD group were cautiously interpreted as positive signs reflecting a good parent–infant relationship, and wellbeing of the children.

Psychological follow-up

In many European countries there has been widespread concern about the potential negative psychological consequences among children conceived by gamete donation. In some countries, e.g. Austria, Germany, Norway, Sweden and Switzerland, the concern is so deep that OD is prohibited by law. Of the various concerns, the impact of keeping information regarding genetic origin secret from the child has raised the greatest debate. Most donor insemination (DI) parents prefer not to tell the child about the method of conception. Oocyte recipients appear to be more open than DI parents and 20–70% intend to tell the child about the nature of their conception (Kirkland et al., 1992; Munro et al., 1992; Weil et al., 1994; Söderström-Anttila, 1998). However, this means that many children resulting from gamete donation grow up without knowing that their mother or father has no genetic link to them. What do we know about the outcome in these families? In a study carried out in the UK (Golombok et al., 1995) greater emotional involvement in parenting among DI parents was reported than among parents with a naturally conceived child. There were no differences in the quality of parent–child relationship between DI parents and either adoptive or IVF parents. These results were confirmed in an extensive European study of family function in different types of assisted reproduction families compared with families with a naturally conceived child (Golombok et al., 1996). Mothers of children conceived by DI or IVF expressed greater warmth towards their children and interacted more with their child than mothers who conceived naturally. The children in these different family types were functioning well and they did not differ as regards the presence of a psychological disorder, emotions, behaviour or relationships with parents. Later, the same group extended their studies to include family function in OD families in comparison with DI families, adoptive families and IVF families (Golombok et al., 1999). A total of 21 OD families were studied and only one child had been told about its manner of conception. Greater psychological wellbeing among mothers and fathers was noticed in families where the mother was genetically unrelated to her child. The families did not differ with respect to the quality of parenting or the psychological adjustment of the child.

Follow-up studies of health status and wellbeing of OD offspring are few, possibly because there may be concern about how the parents will react or if it is ethically correct to regard these families as a risk group. It has appeared that fear of disclosure is the reason why many DI parents do not want to participate in follow-up studies. However, in some studies, oocyte recipient couples have shown themselves to be not only willing but even eager to provide information about their experiences (Applegarth et al., 1995; Söderström-Anttila et al., 1998). There is a great need for more systematic data regarding OD children to be published in order to provide prospective parents, healthcare professionals and policy-makers with essential information about the outcome of these children. The aforementioned studies of DI and OD families with children up to the age of 8 years show that in these families the quality of parenting is superior to that of families with a naturally conceived child and that the children are doing well.

Motherhood at any age?

In Western societies a large number of women choose to delay childbearing in order to fulfill educational goals before trying to begin a family. Furthermore, a high number of divorces and second marriages have contributed to an increasing number of perimenopausal women desiring pregnancy. However, the success rate of assisted reproduction methods is low in women aged >40 years using their own oocytes (Marcus and Brinsden, 1996). OD represents an option that serves these women well. It has been used in women up to the age of 63 years (Antinori et al., 1995; Paulson et al., 1997). However, is such a practice justifiable or should there be an upper age limit of the recipient? One matter of concern has been the psychological well-being of a child in a family with ageing parents. It has been argued that the increased difference in age between parents and children may lead to an increased ‘generation gap’. However, it is not uncommon for children to be raised by their grandparents if both parents have died as a result of illness or accident (Paulson, 1995). It can also be assumed that the life expectancy of parents aged 40–50 years is adequate to raise a child to adulthood. Older couples may also have more time to spend with the children than younger ones. On the other hand, there may come a point in life when raising a child becomes problematic. Thus far, we do not have much experience of the short- and long-term consequences in these families. Ageing recipient candidates need extensive counselling in which the psycho–social effects of the procedure and the best interest of the child-to-be are taken into thorough consideration. As discussed earlier, the health risks of pregnant post-menopausal women should be taken seriously and may constitute sufficient reason to consider an upper age limit of 50–55 years for oocyte recipients.

Conclusions

Evaluation of outcome of children born after OD includes both medical and psychological aspects. Growth and medical health in these children appear to be within normal ranges. Complications related to multiple pregnancies can be avoided by reducing the number of embryos transferred. Such a policy requires, of course, well-functioning embryo cryopreservation systems. In selected cases, i.e. when the oocyte donor is young, the embryo quality is good and the recipient woman has specific obstetric risks, replacement of only one embryo at a time should be considered.

The psychological consequences of OD on the child are difficult to evaluate, because there are so few substantive data on OD families available. The children investigated have been aged <10 years. Studies thus far carried out have revealed overall normal socio–emotional development in the child and positive parent–child relationships.
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References


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