

Donor age is a major determinant of success of oocyte donation/recipient programme

Yueping Alex Wang^{1,*}, Cindy Farquhar², and Elizabeth Anne Sullivan¹

¹Perinatal and Reproductive Epidemiology Research Unit, University of New South Wales, Sydney, Australia ²Department of Obstetrics and Gynaecology, Private Bag, University of Auckland, Auckland, New Zealand

*Correspondence address. Perinatal and Reproductive Epidemiology Research Unit, Level 2, McNevin Dickson Building, Randwick Hospitals Campus, Randwick NSW 2031 Australia. Tel: +61-2-9382-1014; Fax: +61-2-9382-1025; E-mail: alex.wang@unsw.edu.au

Submitted on May 22, 2011; resubmitted on September 18, 2011; accepted on September 30, 2011

BACKGROUND: In recent years, particularly in developed countries, women have tended to delay childbirth until over 40 years of age. Our study aims to identify whether the donor's age or recipient's age influences the pregnancy and live birth rate following oocyte recipient cycles.

METHODS: A population study included 3889 fresh oocyte recipient cycles. Pregnancy and live delivery rates were compared in recipient age groups (<35, 35–39, 40–44 and ≥45 years) and donor age groups (<30, 30–34, 35–39 and ≥40 years).

RESULTS: The highest live birth rate was of cycles in donors aged 30–34 years (25.0%), it decreased ($P < 0.05$) to 24.1% in donors aged <30 years, 20.7% in donors aged 35–39 years and 11.5% in donors aged ≥40 years. The multivariate analysis showed no significant differences in the success by recipient's age. Compared with cycles in donors aged 30–34 years, cycles in donors aged 35–39 years had 14 and 18% less chance to achieve a pregnancy [adjusted rate ratio (ARR) 0.86, 95% confidence interval (CI) 0.75–0.98] and a live delivery (ARR 0.82, 95% CI 0.71–0.96), while cycles in donors aged 40 years or older had 42 and 54% less chance to achieve a pregnancy (ARR 0.58, 95% CI 0.41–0.84) and a live delivery (ARR 0.46, 95% CI 0.29–0.73).

CONCLUSIONS: Older recipients with younger donors did not have a poorer pregnancy outcome compared with younger recipients with younger donors. Choosing a donor aged <35 years would increase the chance of pregnancy and live delivery for older recipients.

Key words: oocyte recipient / recipient age / donor age / live delivery / pregnancy loss

Introduction

It is well established that younger women have high rates of pregnancy and live birth after both spontaneous conception and assisted reproduction treatment (ART) than older women (Menken *et al.*, 1986; Heffner, 2004; Joseph *et al.*, 2005). However, in recent years particularly in developed countries, there has been a trend of women delaying childbirth well into their fourth decade. The latest Australian report shows that about one in seven (14.5%) first-time mothers in 2008 were aged ≥35 years compared with 9.5% in 1999. Similarly, the average age of first-time mothers has increased by 1 year from 27.1 years in 1999 to 28.2 years in 2005 (Laws *et al.*, 2010).

This trend of delaying childbirth has been associated with increased utilization of ART. The number of ART cycles has risen by nearly 50%, from 41 904 in 2004 to 61 929 in 2008 in Australia and New Zealand (Wang *et al.*, 2010). There has also been a trend to seek ART at a later age and more recently, to seek donated oocytes/embryos. In Australia and New Zealand, the proportion of non-donor fresh

cycles in women aged ≥40 years has risen from 21.7% in 2002 to 26.6% in 2008. Donor cycles have increased by 72% from 1733 in 2002 to 2977 in 2008 (Wang *et al.*, 2010). Similar trends have been observed in the UK, where the proportion of cycles in women aged ≥40 years has increased from 9.1% in 1991 to 19.4% in 2008 (Human Fertilisation and Embryology Authority, 2010).

A woman's age is an independent factor for successful pregnancy and perinatal outcomes (Heffner, 2004; Joseph *et al.*, 2005). Advancing age not only leads to declining fertility by reducing the quality of oocytes, reducing uterine receptiveness and lowering of female hormones (Tufan *et al.*, 2004; Baird *et al.*, 2005), but also other chronic health conditions (such as diabetes and hypertension) may complicate pregnancy (Tufan *et al.*, 2004; Alshami *et al.*, 2010). With the increase in a woman's age, the fertility rate in the general population decreases from 400 pregnancies per 1000 married women aged <30 years to 100 per 1000 married women aged 45 years or older (Menken *et al.*, 1986; Heffner, 2004). The miscarriage rate increases with increasing age, from 13% in women in their 20s and early 30s to

>50% in women aged 40 years or older (Nybo Andersen et al., 2000).

Age-related infertility is not only attributable to the women but also their male partners. Advanced male age is associated with reducing quantity and quality of sperm (Levitas et al., 2007). Sperm motility was found to be inversely related to advancing age with peak motility of sperm at age <25 years and lowest motility at age ≥ 55 years (Levitas et al., 2007). Interestingly, it has been suggested that the male partner's age has little impact on pregnancy and birth outcomes following ART (Duran et al., 2010).

Not surprisingly, advanced woman's age is a strong predictor of pregnancy and live birth following ART (Ciray et al., 2004; Wang et al., 2008). Although the success rate of ART has improved in recent years, this has not been seen among older women (Ciray et al., 2004; CDC, 2006). The unchanged success rate of non-donor cycles among older women is largely attributable to diminished oocyte quality (Hourvitz et al., 2009). The quality of oocytes determines the outcome of IVF and subsequent pregnancy/birth outcomes (Navot et al., 1991). For this reason, studies have suggested oocyte donation/recipient programmes (ODRP) as being an alternative way to improve the success of ART among older women (Sullivan, et al., 2008; Hourvitz et al., 2009).

In Australia and New Zealand, oocyte/embryo donation/recipient programmes account for $\sim 5\%$ of all ART cycles (Wang et al., 2010). The small proportion of ODRP in Australia and New Zealand are overseen by the Reproductive Technology Accreditation Committee (RTAC). The altruistic 'known donor' model is more frequently used by clinics in Australia and New Zealand. Sisters, cousins, relatives or close friends of reproductive age range are considered as logical oocyte donor candidates (Quinn and Borosh, 2007). In both Australia and New Zealand, oocyte donation can only be altruistic, and donors cannot receive payment apart from their medical costs, in return for their donation (RTAC, 2010). Additionally, fertility centres received advice that patients undergoing autologous treatment should not be approached to donate oocytes (RTAC, 2010). Therefore, egg-sharing programmes are not an option in Australia and New Zealand.

There are no guidelines, uniform policies or recommendations regarding the preferred age for oocyte donors or their recipients in Australia and New Zealand. ODRP varies by state and territory, and by clinic. Population-based evidence of the impact of donor's age on the success of an ODRP is limited. Our study aims to identify whether a donor's age independently determines the success of an ODRP in terms of early pregnancy loss, clinical pregnancy and live delivery. It also investigates the association between the success rate and the interaction of donor's, recipient's and partner's age.

Materials and Methods

Data

Data and definitions used in this study are from the Australian and New Zealand Assisted Reproduction Database (ANZARD), which are maintained at the University of New South Wales. The ANZARD is a census of all initiated ART cycles undertaken in Australia and New Zealand. Items on ANZARD are collected annually, in a de-identified format, from all fertility centres within Australia and New Zealand. The ANZARD includes information on both the ART (oocyte retrieval, IVF and ICSI fertilization procedure, use of thawed embryos, blastocyst

culture, embryo transfer and donation of gametes or embryos) and the resulting pregnancy and birth outcomes (birth status, gestational age, birthweight and congenital anomalies).

A sub-data set of 4142 fresh oocyte recipient cycles undertaken from 1 January 2004 to 31 December 2008 and resulting pregnancy and birth outcomes were extracted from ANZARD. Of these cycles, 36 (0.9%) had donor's age not stated and so were excluded from analysis. A further 217 (5.2%) cycles which intended to use, or used, donor sperm were excluded. A total of 3889 fresh oocyte recipient cycles intended to use or used husband/partner sperm were included in the final analysis.

Study factors

The recipient's age was calculated in completed years at the time of treatment and classified into four groups: <35, 35–39, 40–44 and ≥ 45 years. Donor's age was calculated at the time of oocyte donation and categorized into four groups: <30, 30–34, 35–39 and ≥ 40 years. Husband/partner's age was grouped as <35, 35–39, 40–44 and ≥ 45 years. The cause of infertility was classified as male factor infertility, female factor infertility, combined male-female factor infertility, unexplained infertility and not stated. Previous pregnancy of ≥ 20 weeks gestation was grouped as yes, no and not stated. Stage of embryo development was grouped into cleavage or blastocyst stages. Fertilization procedure was either IVF or ICSI. The number of embryos transferred was grouped as one, two and three or more embryos.

Main outcome measures

A clinical pregnancy was defined as satisfying one of the following criteria: evidence by ultrasound of intrauterine sac(s) or fetal heart(s); examination of products of conception reveal chronic villi; an ectopic pregnancy that had been diagnosed laparoscopically or by ultrasound. A delivery is defined as a birth event in which one or more baby was born at ≥ 20 weeks gestational age or ≥ 400 g birthweight. A live delivery is a birth event in which one or more baby is live born at ≥ 20 weeks gestation or ≥ 400 g birthweight. Pregnancy loss was defined as a clinical pregnancy which had ended before 20 complete weeks of gestation and <400 g birthweight. Ectopic pregnancies and terminations were included.

Statistical analysis

Demographics (donor's age, husband/partner's age, cause of infertility and previous pregnancy of ≥ 20 weeks gestation) and treatment factors (stage of embryo development, fertilization procedure and number of embryos transferred) were compared in various groups of recipient's age. Rates of pregnancy and live delivery were calculated per 100 initiated cycles. Where the number of initiated cycles was not applicable, for example number of embryos transferred, the rates were calculated per 100 embryo transfer cycles. Pregnancy loss rate was measured per 100 clinical pregnancies. Obstetric outcomes were measured per 100 deliveries. Chi-square test was used to measure the association between the outcomes and the interactions of donor's age and recipient's age. Univariate Cox regression was used to investigate the chance of pregnancy, live delivery and pregnancy loss by individual donor's age and recipient's age group. Multivariate Cox regression was used to overcome the influence of other potential demographic and treatment confounders. Rates ratio (RR) and adjusted RR (ARR) (adjusted for demographic and treatment factors) and 95% confidence intervals (95% CIs) were calculated. Data were analyzed using the Statistical Package for the Social Sciences software, version 18.0 (IBM Corporation, Somers, NY, USA).

Ethics

Ethics approval for this study was granted by the Human Research Ethics Advisory Panel of the University of New South Wales, Australia.

Results

About 60% of oocyte recipient cycles were in recipients aged ≥ 40 years with a range from 21 to 58 years. More than three quarters of the cycles were of donors aged 30–39 years with the youngest donor aged 18 years and the oldest 49 years. Cycles (22.6%) in recipients aged ≥ 45 years had at least one previous pregnancy ≥ 20 weeks gestation compared with 10% of cycles in recipients aged < 35 years (Table I).

Advancing recipient's age was associated with an increased proportion of ICSI procedure from 58.3% of cycles in recipients aged < 35 years to 70.0% of cycles in recipients aged ≥ 45 years ($P < 0.05$, χ^2 test). A marginally higher proportion of blastocyst transfer was among cycles in older recipients. Overall, double embryo transfer accounted for nearly 55% of embryo transfer cycles ($P < 0.05$, χ^2 test) (Table II).

Of the 3889 recipient cycles, 3441 (88.5%) had embryos transferred, 1183 (30.4%) resulted in a clinical pregnancy and 880 (22.6%) resulted in a live delivery.

Clinical pregnancy and live delivery rates varied by donor age, not recipient age or partner's age. The highest rates of pregnancy and live delivery were of cycles in donors aged 30–34 years. Cycles in

recipients aged ≥ 45 years had pregnancy rate of 32%. Cycles in recipients of other age groups had pregnancy rate around 30%. The live delivery rates ranged from 22.5 to 22.9% among cycles in the four recipient's age groups. With the advancing partner's age, both pregnancy and live delivery rates slightly decreased, but not statistically significant (Supplementary Table SI).

The multivariate analysis showed no significant differences in both pregnancy and live delivery rates by either recipient's age or partner's age. Compared with recipient cycles in donors aged 30–34 years, cycles in donors aged 35–39 years had 14 and 18% less chance to achieve a pregnancy and a live delivery (ARR 0.86 with 95% CI 0.75–0.98, ARR 0.82 with 95% CI 0.71–0.96, respectively), cycles in donors aged 40 years or older had 42 and 54% less chance to achieve a pregnancy and a live delivery (ARR 0.58 with 95% CI 0.41–0.84, ARR 0.46 with 95% CI 0.29–0.73, respectively) (Supplementary data, Table SI). Similarly, advanced donor's age (35–39 and ≥ 40 years) was associated with lower rates of pregnancy and live delivery per embryo transfer cycle (Table III). There were no significant differences in pregnancy and live delivery rates between donor's age 30–34 and < 30 years, for both recipient cycles (Supplementary data, Table SI) and embryo transfer cycles (Table II).

Of the 1183 clinical pregnancies, 1174 had complete pregnancy outcomes and 9 (0.8%) had unknown outcomes. The pregnancy loss rate was 27.7% for recipients aged ≥ 45 years, higher than the rate of recipients in other age groups (around 23.3%), but not statistically

Table I Selected demographics of participants in the oocyte recipient cycles.

	Recipient's age group (years)				
	≤ 34 ($n = 634$), (%)	35–39 ($n = 942$), (%)	40–44 ($n = 1458$), (%)	≥ 45 ($n = 855$), (%)	All ages ($n = 3889$), (%)
Donor's age group (years)					
<30	23.8	13.3	17.0	24.6	18.9
30–34	41.6	38.3	37.8	38.9	38.8
35–39	33.1	44.1	40.0	31.9	38.1
≥ 40	1.4	4.4	5.2	4.6	4.2
Partner's age group (years)					
<35	59.1	14.2	7.8	5.5	17.2
35–39	24.6	41.1	22.5	12.9	25.2
40–44	6.0	26.0	34.4	23.7	25.4
≥ 45	1.1	9.4	25.0	43.7	21.4
Not stated	9.1	9.2	10.4	14.2	10.7
Cause of subfertility					
Male factor only	12.9	14.4	16.1	14.5	14.8
Female factor only	51.9	41.6	38.5	39.1	41.6
Combined male/ female factor	15.1	17.9	17.5	15.6	16.8
Unexplained	11.4	15.7	17.4	17.1	15.9
Not stated	8.7	10.3	10.5	13.8	10.9
Previous pregnancy of ≥ 20 weeks gestation					
None	83.3	82.8	78.3	71.2	78.7
Yes	10.7	12.8	16.0	22.6	15.8
Not stated	6.0	4.4	5.6	6.2	5.5

Table II Treatment factors of oocyte recipient cycles where embryos were transferred.

	Recipient's age group (years)									
	≤34 (n = 566)		35–39 (n = 836)		40–44 (n = 1283)		≥45 (n = 756)		All age (n = 3441)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Fertilization procedure										
ICSI*	330	58.3	520	62.2	838	65.3	529	70.0	2217	64.4
Stage of embryo development										
Blastocyst*	118	20.8	179	21.4	318	24.8	209	27.6	824	23.9
Number of embryo transferred										
1	276	48.8	341	40.8	523	40.8	364	48.1	1504	43.7
2	282	49.8	486	58.1	734	57.2	381	50.4	1883	54.7
≥3	8	1.4	9	1.1	26	2.0	11	1.5	54	1.6

$P < 0.05$, χ^2 *test (degrees of freedom = 3).

Table III Pregnancy and live delivery rates of oocyte recipient cycles where embryos were transferred by demographic.

	Pregnancy			Live delivery		
	Rate (%)	RR (95% CI)	ARR (95% CI)	Rate (%)	RR (95% CI)	ARR (95% CI)
Recipient's age (years)						
<35	34.3	1.00	1.00	25.6	1.00	1.00
35–39	33.7	0.98 (0.82–1.18)	1.02 (0.84–1.25)	25.4	0.99 (0.80–1.22)	1.08 (0.86–1.37)
40–44	33.7	0.98 (0.83–1.17)	1.04 (0.86–1.27)	25.6	1.00 (0.82–1.21)	1.11 (0.89–1.40)
≥45	36.2	1.06 (0.88–1.27)	1.14 (0.92–1.41)	25.8	1.01 (0.81–1.25)	1.12 (0.87–1.45)
Donor's age (years)						
<30	35.4	0.95 (0.81–1.11)	0.94 (0.81–1.10)	27.4	0.97 (0.81–1.16)	0.98 (0.82–1.17)
30–34	37.3	1.00	1.00	28.1	1.00	1.00
35–39	32.2	0.86 (0.76–0.98)*	0.87 (0.76–0.99)**	23.4	0.83 (0.71–0.97)*	0.83 (0.71–0.96)**
≥40	22.7	0.61 (0.43–0.87)*	0.61 (0.43–0.87)**	13.5	0.48 (0.30–0.76)*	0.48 (0.30–0.76)**
Partner's age (years)						
<35	36.2	1.00	1.00	28.6	1.00	1.00
35–39	35.7	0.99 (0.83–1.17)	0.97 (0.81–1.18)	26.4	0.92 (0.76–1.13)	0.90 (0.72–1.11)
40–44	34.3	0.95 (0.80–1.13)	0.93 (0.76–1.14)	24.8	0.87 (0.71–1.06)	0.84 (0.67–1.06)
≥45	32.7	0.90 (0.75–1.09)	0.87 (0.70–1.08)	24.7	0.86 (0.70–1.06)	0.83 (0.64–1.06)
Not stated	31.8	0.88 (0.70–1.10)	0.92 (0.68–1.23)	22.4	0.78 (0.60–1.02)	0.81 (0.57–1.15)

RR, rates ratio, CI, confidence interval, ARR, adjusted rates ratio.

* $P < 0.05$ in univariate Cox regression model.

** $P < 0.05$ in multivariate Cox regression model (adjusted for recipient's age, donor's age, husband/partner's age, cause of infertility, previous pregnancy of ≥20 weeks gestation, fertilization procedure, stage of embryo development and number of embryos transferred).

significant. The rate of pregnancy loss varied from 20.1 to 26.7% among partner age groups. Even though 12 of 31 pregnancies (38.7%) with donor's aged ≥40 years ended before 20 weeks of gestation, the multivariate analysis did not show a significant difference from the 22.4% pregnancy loss rate in donors aged <30 years, owing to small number of pregnancies following oocyte recipient cycles in donor aged ≥40 years (Supplementary Table SII).

Table IV presents the obstetric outcomes by recipient age groups. Of the 887 deliveries for all age groups, 18.3% were multiple deliveries. There were no significant differences in the rates of preterm birth, low birthweight and multiple delivery by recipient's age group. The Caesarean section delivery rate increased with advancing recipient's age, from 68.2% for recipients aged <35 years to 81.6% for recipients aged ≥45 years.

Table IV Obstetric outcomes (%) following oocyte recipient cycles, by demographic.

	Recipient's age (years)								P-value (χ^2 test)
	<35 (n = 148)		35–39 (n = 213)		40–44 (n = 330)		≥45 (n = 162)		
	No.	%	No.	%	No.	%	No.	%	
Multiple delivery	28	18.9	38	17.8	62	18.8	34	17.3	0.97
Preterm birth	38	25.7	55	25.8	79	23.9	55	28.1	0.78
Any low birthweight	32	21.6	49	23.0	62	18.8	43	21.9	0.65
Caesarean section	101	68.2	147	69.0	258	78.2	160	81.6	<0.01

Discussion

This population study concluded that donor's age had the largest impact on pregnancy and live delivery rates following fresh oocyte recipient cycles. Cycles with donor age of 35–39 years and ≥ 40 years were associated with 18 and 54%, respectively, lower rates of live delivery compared with cycles with donor aged 30–34 years. An older recipient had a similar chance of successful pregnancy with a young donor as a younger recipient with young donor. There was no significant relationship between the success rates and recipient's age or partner's age. The study suggests that in fresh ODRP, choosing a young donor would increase the chance of pregnancy and live delivery for older recipients.

ODRPs only accounts for a small proportion of ART cycles in most countries (de Mouzon *et al.*, 2010; Wang *et al.*, 2010). Published journal articles on ODRP have limited generalizability because of small sample size and single clinic setting (Zenke and Chetkowski, 2004; Campos *et al.*, 2008). The lack of population-based studies and contemporaneous data makes it difficult to provide adequate evidence on the potential interaction of donor's age with recipient's age and the success of fresh oocyte recipient cycles. Our population cohort study using the most recently available data (2004–2008) of fresh oocyte recipient cycles in Australia and New Zealand overcomes these weaknesses as there is significant study power as well as generalizability.

A limitation of this study is the potential variability in reporting of pregnancy outcomes. The information on pregnancy outcomes was not stated for 9 of the 1183 clinical pregnancies of the study cohort, however, the effect on the results of missing data is likely minimal as it represents a very small percentage (0.8%). It is likely that the missing outcomes would be non-differentially distributed across donor's and recipient's age groups. Secondly, our multivariate analysis controlled for many important potential confounders such as recipient's age, donor's age, husband's/partner's age, cause of infertility, previous pregnancy of ≥ 20 weeks gestation, type of fertilization, stage of embryo development and number of embryo transferred. We were unable to control for other potential confounders related to the oocyte donors, such as FSH level, anti-Müllerian hormone level or ovarian size, and those related to the recipients such as BMI, length of infertility, history of oral contraceptive use, estradiol level or endometrial preparation (Soares *et al.*, 2005).

Our results are in agreement with early published papers showing that recipient age was not associated with pregnancy and live delivery outcomes following fresh oocyte recipient cycles (Balmaceda *et al.*, 1994; Abdalla *et al.*, 1997; Noyes *et al.*, 2001). A large early population study from the USA also confirmed a constant success rate among recipients aged 25 years through those in their late 40's (Toner *et al.*, 2002). However, a recently published study suggested that recipients aged ≥ 39 years had lower pregnancy rate than their younger counterpart (Campos *et al.*, 2008); the conflicting results between the Campos study and ours could be explained by their small study size (915 cycles) and single population source from a single institute, compared with our study of 3889 cycles from all clinics in Australia and New Zealand.

Studies have shown that both oocyte quality and uterine conditions may diminish with advancing age (Tufan *et al.*, 2004; Baird *et al.*, 2005). The lower fertility rate in older women may be explained by the combination of the quality of oocyte and uterine conditions. An ODRP provides a good model to examine the impact of the uterine/endometrial conditions related to pregnancy and live birth by eliminating the effect of oocyte quality. The similar rates of pregnancy, pregnancy loss and live delivery among recipients aged <35, 35–39, 40–44 and ≥ 45 years suggests that uterine conditions have less effect on outcomes of fresh oocyte recipient cycles than oocyte quality. This point is further strengthened by those studies where oocyte quality was controlled, as they have reported that conception and ongoing pregnancy rates appear to be independent of uterine age (Balmaceda *et al.*, 1994; Navot *et al.*, 1994; Abdalla *et al.*, 1997; Noyes *et al.*, 2001; Check *et al.*, 2010).

If uterine conditions do have a negative impact on the success, it appears to only occur with recipients aged in their late 1940s and early 1950s. Balmaceda *et al.* (1994) suggested that there are no substantial uterine changes in terms of receptivity, embryo implantation and nidation maintenance before 53 years of age. Others have reported lower success rates for recipients aged ≥ 45 years than their younger counterparts (Toner *et al.*, 2002; Soares *et al.*, 2005). Most women go through natural menopause in their late 1940s or early 1950s. The endocrine profiles of peri- and post-menopausal women are different from premenopausal women. Conception in women in their late 1940s or early 1950s is possible with the help of hormonal replacement therapy and proper endometrial preparation, which are not used in premenopausal women (Saunders and

Bowman, 1995). In fact, our study did not find a significant impact of recipient's age ≥ 45 years on pregnancy and live delivery rates and it would seem that the addition of exogenous hormones does not adversely impact on pregnancy outcomes. The ANZARD does not collect menopausal status and therefore we were unable to investigate the interaction between uterine age and natural menopause, as well as the different endometrial preparation protocol for pre- and post-menopausal recipients, on the pregnancy outcomes.

Even though advanced recipient age did not have an impact on pregnancy and live delivery rates in our study, other authors have reported that older recipients are more likely to have an increased risk of maternal and obstetric complications (Soares et al., 2005). Hypertension, proteinuria and antepartum hemorrhage were more common among recipients aged ≥ 45 years than those aged < 45 years (Soares et al., 2005). Our study was unable to assess maternal complications as this data was not collected by ANZARD.

The majority of women who use donor oocytes have absent ovaries or diminished ovarian reserve, poor oocyte quality, early menopause, premature ovarian failure and chromosomal or genetic disorders (Toner et al., 2002). Increasingly, women with advanced age or women who have had repeated failure of autologous ART or recurrent miscarriages are seeking donated oocytes (Soares et al., 2005; Quinn and Borosh, 2007). Notably in our study, 38% of cycles were in recipients aged 40–44 years and 22% of cycles were in recipients aged ≥ 45 years. Any female factor infertility was reported for more than half of cycles with ovarian-related infertility for 31% of cycles, other female factor infertility for 8.6% of cycles and combined male and female factor infertility for 16.8% of cycles. Interestingly, 14.8% of cycles had male factor as the only cause of infertility. This was probably related to advanced recipient age because 62% of cycles with male factor infertility were in recipients aged ≥ 40 years compared with 55% of cycles with female factor infertility. The recipient's age correlated with male partner's age, and advancing male age was associated with decreasing in male fertility (Levitas et al., 2007).

Consistent with other studies we did not find that advanced male age was associated with a decrease in the likelihood of pregnancy and live delivery (Duran et al., 2010; Whitcomb et al., 2011), even though increased male age is known to be associated with reduced semen volume and motility (Levitas et al., 2007). It is possibly related to the methods and procedures used to address male factor infertility, namely epididymal sperm aspiration/testicular sperm extraction and ICSI procedure. In our study of cycles in husbands/partners aged ≥ 45 years, 11% had sperm collected by surgical retrievals from either the epididymides or testes. We also found that the proportion of ICSI procedures was significantly higher among husbands/partners aged ≥ 45 years (70%) than those husbands/partners aged < 35 –44 years (59%) and < 35 years (50%). Once male factor infertility is overcome, clinical pregnancy, implantation, miscarriage and live birth rates were not affected by advanced male age (Duran et al., 2010).

Some recent studies have discussed the improvement of the success of ART, including ODRP (Sullivan, et al., 2008; Hourvitz et al., 2009; Borini et al., 2011). An Australian study reported that, in women aged ≥ 45 years, the live birth rate of 19.1% was significantly higher for fresh oocyte recipient cycles than the rate of 0.5% for fresh autologous cycles (Sullivan et al., 2008). The high rates of clinical pregnancy and live delivery and lower rate of pregnancy loss following

ODRP than autologous treatment suggested ODRP is an alternative option to improve the success (Borini et al., 2011). However, the ODRP is far more complicated than autologous treatment. Legislation, policies and recommendations regarding eligibility, including preferred age limits, ethics, acceptance, payment, safety of both donors and recipient, and disclosure of the identity of the biological mother), need to be established and addressed prior to donation (Kramer et al., 2009; van der Hoorn, 2010; Lindheim et al., 2011).

In Australia and New Zealand, there are no national recommendations on limiting the woman's age for receiving oocytes. An early Australian study suggested an upper age limit of 50 years, with each case being examined on its own merits and without fixed rules (Saunders and Bowman, 1995). Recent international studies have proposed that there is a better chance of pregnancy for recipients' < 45 years of age (Toner et al., 2002; Soares et al., 2005). We did not find a significant decline in pregnancy and live delivery rates for recipient's ≥ 45 years of age. This suggests there is no evidence to support a fixed cut-off for preferred age to receive oocytes.

An early study suggested that the implantation rate started to decrease in donors aged 36 years and onwards (Balmaceda et al., 1994). Owing to lack of information on number of gestational sacs, we were unable to calculate the implantation rate. The slightly higher pregnancy and live delivery rates for cycles with donors aged 30–34 years compared with donors aged < 30 years (not statistically significant) provides evidence that the association of age of donor with better outcome is not linear. Our data suggest that choosing a younger donor increases the chance of a live birth, ideally a donor aged 30–34 years. However, this does not reflect the current ODRP in Australia and New Zealand. We found that 42% of fresh recipient cycles were of donors aged ≥ 35 years. The relative higher proportion of cycles with older donors is probably associated with the 'known donor' model in Australia and New Zealand (Quinn and Borosh, 2007). It might also be related to the fact that the age of the oocyte donor has been correlated with the age of the recipient (Toner et al., 2002).

The delay in childbirth in the general population and less favorable outcomes among older women suggests that the current trends of postponing childbearing are inadvisable at a population level. ART, while one option, is not a guarantee of parentage, and oocyte cryopreservation to avoid age-related infertility is another option (Stoop et al., 2011) but once again with few guarantees of success (Oktay et al., 2006). Instead, better community education about fertility potential and the impact of advancing maternal age on both natural and assisted conception is needed (Sullivan et al., 2008).

Supplementary data

Supplementary data are available at <http://humrep.oxfordjournals.org/>.

Authors' roles

Y.A.W. was involved in study design, method investigation, data analysis and preparing the manuscript. C.F. was involved in study design, method investigation and review and editing of the manuscript. E.A.S. was involved in study design, method investigation and review of the manuscript.

Acknowledgements

The authors acknowledge the contribution of Australian and New Zealand fertility clinics in the provision of data to ANZARD.

Conflict of interest

We have no conflict of interest in relation to this work. All authors have contributed to the conducting of this study. The manuscript has been seen and approved by all authors. The order of authorship was agreed by all authors.

Funding

The Fertility Society of Australia is the funding body for the ANZARD.

References

- Abdalla HI, Wren ME, Thomas A, Korea L. Age of the uterus does not affect pregnancy or implantation rates; a study of egg donation in women of different ages sharing oocytes from the same donor. *Hum Reprod* 1997;**12**:827–829.
- Alshami HA, Kadasne AR, Khalfan M, Iqbal SZ, Mirghani HM. Pregnancy outcome in late maternal age in a high-income developing country. *Arch Gynecol Obstet* 2010; Epub ahead of print, DOI: 10.1007/s00404-010-1821-6.
- Baird DT, Collins J, Egozcue J, Evers LH, Gianaroli L, Leridon H, Sunde A, Templeton A, Van Steirteghem A, Cohen J et al. Fertility and ageing. *Hum Reprod Update* 2005;**11**:261–276.
- Balmaceda JP, Bernardini L, Ciuffardi I, Felix C, Ord T, Sueldo CE, Asch RH. Oocyte donation in humans: a model to study the effect of age on embryo implantation rate. *Hum Reprod* 1994;**9**:2160–2163.
- Borini A, Suriano R, Barberi M, Dal Prato L, Bulletti C. Oocyte donation programs: strategy for improving results. *Ann N Y Acad Sci* 2011;**1221**:27–31.
- Campos I, Gómez E, Fernández-Valencia AL, Landeras J, González R, Coy P, Gadea J. Effects of men and recipients' age on the reproductive outcome of an oocyte donation program. *J Assist Reprod Genet* 2008;**25**:445–452.
- CDC. 2004 Assisted Reproductive Technology Success Rates. Atlanta, GA, USA: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, 2006.
- Check JH, Katsoff B, Jamison T, Choe JK, Brasile D, Amui J. A novel method to assess the effect of uterine senescence by comparing pregnancy outcome in younger donors vs older recipients who are sharing a common pool of oocytes. *Clin Exp Obstet Gynecol* 2010;**37**:97–98.
- Ciray HN, Ulug U, Bahceci M. Transfer of early-cleaved embryos increases implantation rate in patients undergoing ovarian stimulation and ICSI-embryo transfer. *Reprod Biomed Online* 2004;**8**:219–223.
- de Mouzon J, Goossens V, Bhattacharya S, Castilla JA, Ferraretti AP, Korsak V, Kupka M, Nygren KG, Nyboe Andersen A; European IVF-monitoring (EIM) Consortium, for the European Society of Human Reproduction and Embryology (ESHRE). Assisted reproductive technology in Europe, 2006: results generated from European registers by ESHRE. *Hum Reprod* 2010;**25**:1851–1862.
- Duran EH, Dowling-Lacey D, Bocca S, Stadtmayer L, Oehninger S. Impact of male age on the outcome of assisted reproductive technology cycles using donor oocytes. *Reprod Biomed Online* 2010;**20**:848–856.
- Heffner LJ. Advanced maternal age—how old is too old?. *N Engl J Med* 2004;**351**:1927–1929.
- Hourvitz A, Machtinger R, Maman E, Baum M, Dor J, Levron J. Assisted reproduction in women over 40 years of age: how old is too old?. *Reprod Biomed Online* 2009;**19**:599–603.
- Human Fertilisation and Embryology Authority (HFEA). Fertility Facts & Figures 2008. Publication date 08 December 2010 Version 1.0. http://www.hfea.gov.uk/docs/2010-12-08_Fertility_Facts_and_Figures_2008_Publication_PDF.PDF (30 March 2011, last date accessed).
- Joseph KS, Allen AC, Dodds L, Turner LA, Scott H, Liston R. The perinatal effects of delayed childbearing. *Obstet Gynecol* 2005;**105**:1410–1418.
- Kramer W, Schneider J, Schultz N. US oocyte donors: a retrospective study of medical and psychosocial issues. *Hum Reprod* 2009;**24**:3144–3149.
- Laws PJ, Li Z, Sullivan EA. *Australia's Mothers and Babies 2008*. Perinatal statistics series no. 24. Cat. no. PER 50. Canberra: AIHW, 2010.
- Levitas E, Lunenfeld E, Weisz N, Friger M, Potashnik G. Relationship between age and semen parameters in men with normal sperm concentration: analysis of 6022 semen samples. *Andrologia* 2007;**39**:45–50.
- Lindheim SR, Porat N, Jaeger AS. Survey report of gamete donors' and recipients' preferences regarding disclosure of third party reproduction outcomes and genetic risk information. *J Obstet Gynaecol Res* 2011;**37**:292–299.
- Menken J, Trussell J, Larsen U. Age and fertility. *Science* 1986;**233**:1389–1394.
- Navot D, Bergh PA, Williams MA, Garrisi GJ, Guzman I, Sandler B, Grunfeld L. Poor oocyte quality rather than implantation failure as a cause of age-related decline in female fertility. *Lancet* 1991;**337**:1375–1377.
- Navot D, Drews MR, Bergh PA, Guzman I, Karstaedt A, Scott RT Jr, Garrisi GJ, Hofmann GE. Age-related decline in female fertility is not due to diminished capacity of the uterus to sustain embryo implantation. *Fertil Steril* 1994;**61**:97–101.
- Noyes N, Hampton BS, Berkeley A, Licciardi F, Grifo J, Krey L. Factors useful in predicting the success of oocyte donation: a 3-year retrospective analysis. *Fertil Steril* 2001;**76**:92–97.
- Nybo Andersen AM, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: population based register linkage study. *Br Med J* 2000;**320**:1708–1712.
- Oktay K, Cil AP, Bang H. Efficiency of oocyte cryopreservation: a meta-analysis. *Fertil Steril* 2006;**86**:70–80.
- Quinn F, Borosh C. Oocyte donation in assisted conception. *O&G Magazine* 2007;**9**:12–13.
- Reproductive Technology Accreditation Committee (RTAC). *Code of Practice for Assisted Reproductive Technology Units*. Melbourne: Fertility Society of Australia, 2010.
- Saunders S, Bowman M. The upper age limit for egg donation recipients. *J Assist Reprod Genet* 1995;**12**:230–232.
- Soares SR, Troncoso C, Bosch E, Serra V, Simón C, Remohí J, Pellicer A. Age and uterine receptiveness: predicting the outcome of oocyte donation cycles. *J Clin Endocrinol Metab* 2005;**90**:4399–4404.
- Stoop D, Nekkebroeck J, Devroey P. A survey on the intentions and attitudes towards oocyte cryopreservation for non-medical reasons among women of reproductive age. *Hum Reprod* 2011;**26**:655–661.
- Sullivan EA, Wang YA, Chapman M, Chambers G. Success rates and cost of a live birth following fresh assisted reproduction treatment in women aged 45 years and older, Australia 2002–2004. *Hum Reprod* 2008;**23**:1639–1643.
- Toner JP, Grainger DA, Frazier LM. Clinical outcomes among recipients of donated eggs: an analysis of the U.S. national experience, 1996–1998. *Fertil Steril* 2002;**78**:1038–1045.

- Tufan E, Elter K, Durmusoglu F. Assessment of reproductive ageing patterns by hormonal and ultrasonographic ovarian reserve tests. *Hum Reprod* 2004;**19**:2484–2489.
- van der Hoorn ML, Lashley EE, Bianchi DW, Claas FH, Schonkeren CM, Scherjon SA. Clinical and immunologic aspects of egg donation pregnancies: a systematic review. *Hum Reprod Update* 2010;**16**:704–712.
- Wang YA, Healy D, Black D, Sullivan EA. Age-specific success rate for women undertaking their first assisted reproduction technology treatment using their own oocytes in Australia, 2002–2005. *Hum Reprod* 2008;**23**:1633–1638.
- Wang YA, Chambers GM, Sullivan EA. *Assisted Reproductive Technology in Australia and New Zealand 2008*. Assisted reproduction technology series no. 14. Cat. no. PER 49. Canberra: AIHW, 2010.
- Whitcomb BW, Turzanski-Fortner R, Richter KS, Kipersztok S, Stillman RJ, Levy MJ, Levens ED. Contribution of male age to outcomes in assisted reproductive technologies. *Fertil Steril* 2011;**95**:147–151.
- Zenke U, Chetkowski RJ. Transfer and uterine factors are the major recipient-related determinants of success with donor eggs. *Fertil Steril* 2004;**82**:850–856.