Reproduction beyond menopause: how old is too old for assisted reproductive technology?

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Abstract

Background Due to the recent media attention on postmenopausal women giving birth, there has been an increased scrutiny on the utility and safety of assisted reproductive technology in postmenopausal women.

Objective The purpose of this commentary is to discuss the following: 1) the limitations and complications of ART in women of advanced reproductive age; 2) the balance between the welfare of the mother and that of the child; 3) the double standards of advanced reproductive age; and 4) the importance of financial and social support systems and preconception counseling with advanced reproductive age.

Conclusion When providing in-vitro fertilization services to women of advanced reproductive age, special considerations must be given to ensure the welfare of mother and the child and that the principles of beneficence and nonmaleficence are guaranteed.

Keywords Ethics · In-vitro fertilization · Postmenopausal reproduction · Child welfare

Introduction

The publicity surrounding the recent case of Maria Bousada, the 66-year-old single mother who died 3 years after conceiving with donor eggs from an in-vitro fertiliza-

tion (IVF) facility in California, leaving behind her 2-year-old orphaned twins, sparked an ethical debate on age restrictions for access to infertility treatment [1]. There is also the case of Omkari Panwar, who is the oldest woman to give birth to twins at the age of 70, using donor eggs from an IVF facility in India [2]. Despite the different cultures, it is evident that the desire to reproduce, by any means, is very important, especially since biblical times as witnessed with Genesis 1:28—“Be fruitful and multiply.” Concerns for assisting patients over the age of 50 in their desire to have children stems from their shortened life expectancies, with the children likely losing one or both parents prior to reaching adulthood. The recent media attention surrounding these cases has cast a negative light on the practices of IVF facilities and may set the stage for future regulation of these practices. To deter future regulation, reproductive endocrinologists and their IVF facilities need to be more diligent in screening older patients seeking assisted reproductive technologies (ART) using donor eggs.

With the use of donor eggs, women 50 years of age and older are able to conceive with ART [3–6]. To the credit of many physicians and their IVF facilities, they have regulated their own practices by setting their own criteria for women of advanced reproductive age. Nevertheless, despite diligence by the majority of IVF facilities in screening older women for IVF, the unfortunate cases in which older donor egg recipients die before their offspring reach adulthood will likely continue to stir ethical debates.

The crux of this ethical dilemma is the balancing of the interest of the patient’s autonomy for reproductive freedom and that of the child born from a patient of advanced reproductive age. Traditionally, our society promotes a patient’s freedom to naturally reproduce without assistance, even at an advanced age; however, the right to receive reproductive assistance is neither morally nor legally clear-

Capsule Special considerations must be given to patients of 50 years of age and older when providing IVF services to ensure maternal and child welfare.

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cut. Unless these older parents are physically or psychologically unfit, their right to care for their children is generally not restricted. These concerns for the older patient, although appropriate, infringe on their reproductive freedom and impose a double standard. Some will argue that there exists a double standard between men and women, wherein less negative attention is drawn to men who conceive children at an older age compared to women of a similar age. A double standard may exist between the old and the young and between the healthier and the less healthy persons, as well [7].

Nonetheless, the choice of procreation in older patients should not be restricted unless there is sound justification to do so. With science, we often ask if it is possible, but seldom do we ask if we should. Now that IVF with donor eggs can provide the opportunity for patients of advanced reproductive age to give birth, reproductive endocrinologists need to be selective and take extra precautions so as not to place these older patients in a position that could endanger their health during pregnancy and birth. Likewise, special consideration needs to be given to the potential child so it is likely that at least one parent or contingent legal guardian will be available and responsible for the child until that child reaches adulthood.

When offering IVF services to patients, reproductive endocrinologists need to be diligent in balancing the desires of the patient to become pregnant, the potential medical problems the patient may endure during pregnancy, and the best interests of the potential child. There, however, should be a higher scrutiny when providing IVF services to older patients, as their age, pre-existing conditions, and differing family structure are evidently more taxing and their risks more foreseeable. In other circumstances, such as in younger patients, these additional evaluations and considerations for contingency plans and support systems may also be appropriate, depending on their particular conditions.

Age limitations to reproduction

Age limitations to reproduction can be divided into the following categories: physiologic reproductive age, technical capabilities of ART, and social limitations.

The first, physiologic reproductive age, ranges from the age at which ovulation begins, which is generally the age of menarche, to the age at which ovulation ceases, which is that of menopause [8]. Simply enough, the natural course of female reproduction is limited by menopause; however, this physiologic age barrier is transcended by the technical capabilities of ART.

There are social aspects limiting a patient's reproductive potential as well. First and foremost is life expectancy. A woman of advanced reproductive age who dies before her

child's 18th birthday may leave her child without financial support or without a caretaker. According to the CDC's most recent published life tables, at the average age of menopause, 51, a female can expect to live another 31.8 years, and at the age of 68, a female can expect to live another 17.7 years (Table 1) [9]. It can be expected that a 68-year-old woman may not live to her child's 18th year of life, the traditional and legal cutoff for self-sufficiency in the United States. Also, additional predisposing factors may limit her life expectancy even further [10]. Therefore, IVF facilities should select a minimum age at which special considerations for extensive counseling are needed, taking into account that the patient's life expectancy should well exceed 18 years. The authors chose this reasonable cutoff as it is the age of majority, when a person is no longer considered a minor, in the United States; however, this cutoff may not be appropriate and may differ depending on the culture or legal conditions. When determining the need for additional counseling, reproductive endocrinologists

Table 1 CDC life tables for females, Unites States, 2004

Age in Years	Remaining life expectancy in years
20–21	61.2
30–31	51.5
40–41	41.9
50–51	32.7
...	...
51–52	31.8
52–53	30.9
53–54	30.0
54–55	29.1
55–56	28.3
56–57	27.4
57–58	26.5
58–59	25.7
59–60	24.8
60–61	24.0
61–62	23.2
62–63	22.4
63–64	21.6
64–65	20.8
65–66	20.0
66–67	19.2
67–68	18.4
68–69	17.7
69–70	16.9
70–71	16.2
...	...
80–81	9.8
90–91	5.2

should consider the age of the mother, her associated medical complications at that age, and her remaining life expectancy. Furthermore, IVF facilities should perform health-screening evaluations for all females at risk of lowered life expectancies.

In addition to evaluating females with shortened life expectancies, reproductive endocrinologists should consider the age and life expectancy of their partners. Typically, men have shorter life expectancies than women do, and traditionally, men have been the older partners, thus having even shorter life expectancies. For example, whereas a female of 68 years of age can be expected to live for about another 18 years, a 68-year-old male might be expected to live for only another 15 years (Table 2). Therefore, the life expectancy of both parents should be taken into consideration, especially since the life expectancy of the father will become even more important if the mother dies.

Second, physicians have to consider the psychological welfare of the child, especially if the mother has a less-than-

ideal remaining life expectancy. Children who experience the death of a parent, much less an only parent, are at a greater risk for depression, posttraumatic stress disorder, and future drug abuse [11, 12]. This points to the need for an immediate alternate caretaker or guardian to ensure the proper fostering of the child's subsequent psychological development.

Medical complications with advanced reproductive age

As shown by these case reports, the age barrier can be pushed to a completely new limit, but as seen recently in current events, people wonder if this new upper limit is too far. It is important to rehash the dangers of ART in women of advanced reproductive age, as medical complications of pregnancy rise with age. Salihu et al. conducted a retrospective study in 2003 evaluating the survival rate and well being of the fetus stratified by maternal age. The authors concluded that women aged 50 years and older experienced a statistically significant increase in fetal risks during childbearing, which included increased incidences of fetal low birth weight, preterm birth, small for gestational age, and fetal mortality. Salihu et al. also evaluated maternal risks during childbearing stratified by maternal age, again finding a statistically significant increase in maternal morbidity during childbearing, including increased risk of cardiac disease, diabetes, preeclampsia, and placental abruptions in those women greater than 50 years of age [13]. In 2006, Nabukera et al. performed a cross-sectional study that also evaluated maternal and fetal morbidity and mortality during childbearing in women of advanced maternal age [14]. These findings showed statistically significant increases in both maternal and fetal morbidities in those women over the age of 40 years, confirming the findings of Salihu et al. [13]. With these findings of increased maternal risk of childbearing with increasing age, it becomes clear that physiologic menopause occurs as a safety feature to protect against the adverse events of pregnancy in advanced age.

Beneficence and nonmaleficence

Physicians are bound by ethics to uphold the principles of beneficence and nonmaleficence. Beneficence is to provide a benefit to the patient, and nonmaleficence is to do no harm to the patient. Using these 2 principles together, physicians are to act in the best interest of the patient. When discussing reproductive freedom, benefits to the patient can be seen as patient autonomy and patient rights. In addition, both parents will greatly benefit from ART, especially if they have infertility issues and no current

Table 2 CDC life tables for males, United States, 2004

Age in Years	Remaining life expectancy in years
20–21	56.2
30–31	46.9
40–41	37.6
50–51	28.8
...	...
51–52	28.0
52–53	27.2
53–54	26.3
54–55	25.5
55–56	24.7
56–57	23.9
57–58	23.1
58–59	22.3
59–60	21.5
60–61	20.8
61–62	20.0
62–63	19.3
63–64	18.5
64–65	17.8
65–66	17.1
66–67	16.4
67–68	15.7
68–69	15.0
69–70	14.4
70–71	13.7
...	...
80–81	8.2
90–91	4.4

offspring. Nonmaleficence, however, requires physician to protect the patient from harm. As discussed, there are increased risks of complications to both the mother and the fetus with pregnancy at an advanced reproductive age. In this instance, the reproductive endocrinologist has 2 patients: the mother and the child. Therefore, to act in the best interest of both the mother and child, the reproductive endocrinologist should gauge whether the benefits of motherhood and childrearing outweigh the risks of childbearing to the mother and whether such risks may also endanger the welfare of the child. When evaluating older patients for IVF services, physicians should consider the rights of the patients, their physical and mental well being, their remaining life expectancies, and their financial resources and support systems to ensure that they are truly acting not just in the best interests of the parents, but also those of the children.

Double standards in reproduction

Everyone has a natural right to reproduce, but unfortunately for postmenopausal women, this right becomes less natural and more artificial, whereas many older men of the same age group can retain the natural ability to reproduce without the need for ART. Thus, society is less likely to scrutinize older men for fathering children at such an age than they are with older women. In addition, men who conceive at an older age without ART generally have a partner who is well within her reproductive age range, and their children, therefore, will generally have a caretaker in the event the father dies. Although older women may or may not have these same options, physicians should avoid this double standard and consider each patient individually. At the same time, they should keep in mind the best interests of both the patient and the child by avoiding situations that would endanger either. On the other hand, since older men may not need reproductive assistance, the services of IVF facilities may not be needed in such cases. In addition, physicians may reserve the right to refuse any services that they find morally objectionable. The right of physicians to refuse to provide services that they find morally objectionable is supported by the American Medical Association (AMA) code of ethics that states “A physician shall, in the provision of appropriate patient care, except in emergencies, be free to choose whom to serve, with whom to associate, and the environment in which to provide medical care.” [15]

Double standards not only exist between older men and older women, but also between more healthy older women and less healthy younger women. For example, women with BRCA mutations with prophylactic oophorectomies or those with premature ovarian failure may be more likely to receive ART than older women with no medical history and

a family history of long-living relatives. In this instance, the younger women may be afflicted with potentially fatal diseases that could limit their remaining life expectancies; however, there is usually no way of telling that they have a potentially fatal disease, unless physicians screen for them, which is not routinely done. Every situation is unique, and every individual should be evaluated as so. To promote reproductive freedom, this necessitates the individuality of infertility treatment and deterrence of governmental regulations that may forbid ART in menopausal women.

Child welfare and well being

Even though there are exceptional ethical reasons to support reproductive freedom, especially to avoid discrimination and a double standard, there still exist many reasons for a reproductive endocrinologist to be extremely cautious when deciding whether to provide IVF services for women of advanced reproductive age seeking ART. One of these considerations concerns the welfare of the child.

In the United Kingdom, the Human Fertilization and Embryology Authority (HFEA) has set a standard of care known as the Code of Practice, which lends some guidance to the treatment of infertility. Of special note is the section of their Code of Practice on the welfare of the child when seeking infertility treatment. The HFEA does not set an age limit for infertility treatment; however, they do publish guidelines regarding the welfare of the child, which guides the assessment of any infertility treatment for any patient of any age with regard to the future child's welfare, including, but not limited to, surrogacy arrangements, parental risk factors that may cause either physical or psychological harm to the child, and genetic predispositions [16]. Some of their Code of Practice guidelines—verification of identity, establishing parental responsibility, and medical and social history—should be an obvious inclusion in any physician's practice. Verifying a patient's identification, especially their date of birth for age, is essential in establishing the patient's remaining life expectancy and relative physical and mental health. Although some patients, such as Maria Bousada, the 66-year-old single mother who died 3 years after conceiving with donor eggs, have misrepresented their age, it is in the best interest of the physician, the IVF facility, the patient, and the potential offspring if the correct age is known; therefore, every effort within reasonable means should be made to ensure the validity and accuracy of the patient's identification. Reproductive endocrinologists should identify potential custodianship arrangements, whether it is a spouse, a godparent, or other guardian, as a contingency plan for parents of advanced reproductive age. Taking these additional steps to ensure the future welfare of the child is critical.

Financial and social support systems

Childbearing and childrearing are both long periods of emotional stress that, combined with the degenerative aging of a person's physical and mental health, can be detrimental to a child's welfare. Women of advanced reproductive age who seek infertility treatment may have a poor social support system. Given their age, many may not have family who can assist them, especially if they are seeking to have a first child. Thus, it is essential to identify potential caretakers and ensure that the patient has a support system of caretakers during the child's younger years.

As many patients age and enter retirement, their disposable incomes diminish. Some of these patients have Social Security income, and others have retirement pensions from previous or current employment. Nonetheless, those entering or nearing retirement age tend to have less income; therefore, they may lack financial support to support themselves, much less provide for childrearing. Clearly, women of advanced reproductive age are at a number of disadvantaged positions to give birth and raise a child, reinforcing the idea that it is imperative for IVF facilities to identify all support systems to ensure that not only the patient, but also the child, receives adequate care at the present and in the future.

Importance of preconception counseling

For women of advanced reproductive age, obtaining a complete medical and social history is pertinent in determining the state of their physical and mental health. Obviously, the question as to whether an older female can bear a child has been answered with ART and IVF utilizing egg donors; however, IVF facilities need to address the patient's future physical and mental capabilities of being a caretaker to her child. Women of advanced reproductive age are particularly at risk of heart disease, cancer, cerebrovascular disease, and dementia [17–19]; thus, it becomes essential for infertility centers to screen and evaluate for any of these, especially heart disease, since pregnancy itself is physically strenuous [20]. In addition to a medical screening, an extensive psychological evaluation is necessary to elucidate any potential deficiencies in the patient's mental capacity and any psychosocial adversity that may be harmful to the child.

Conclusion

Physicians are bound to the principles of beneficence and nonmaleficence, which should also apply to infertility treatment for women of advanced reproductive age and

the welfare of the child conceived from IVF. Although IVF has made childbearing possible for menopausal women and even though patients generally have an inherent right to reproduce, it may not be in the best interests of a particular patient or their potential offspring to proceed with IVF. Given the medical complications associated with pregnancy, reproductive endocrinologists must be extremely selective in providing ART to women of advanced reproductive age. Special consideration needs to be given to the patient's financial and social support systems and contingency plans in the event of death or disability of one or both parents. Practicing safe medicine by doing no harm and acting in the best interest of not only the patient but any expected children will help deter the government from imposing regulations on reproductive endocrinologists and their IVF facilities.

The authors recommend consideration of the following factors when providing IVF services to patients 50 years of age and older:

1. Remaining life expectancies of both parents should well exceed 18 years.
2. A contingency plan should exist for guardianship in the event of death or illness of one, if a single parent, or both parents.
3. Financial resources are available to support of the child after the parents retire.
4. The patient is referred to a maternal-fetal medicine specialist for evaluation of high-risk pregnancy associated with advanced maternal age.
5. The patient should undergo extensive medical screening, especially cardiac evaluation, including but not limited to stress testing and electrocardiogram.
6. Both parents should undergo psychological evaluation.

References

1. Jones B. Oldest woman to give birth dies, leaving twins. USA Today. July 15, 2009. Available at http://www.usatoday.com/news/world/2009-07-15-spain-oldest-woman-birth_N.htm. Accessed September 27, 2009.
2. Woman in India 'has twins at 70'. BBC News. July 5, 2008. Available at http://news.bbc.co.uk/go/pr/ft/-/2/hi/south_asia/7491782.stm. Accessed September 27, 2009.
3. Check JH, Nowroozi K, Barnea ER, Shaw KJ, Sauer MV. Successful delivery after age 50: a report of two cases as a result of oocyte donation. *Obstet Gynecol*. 1993;81:835–6.
4. Antinori S, Versaci C, Gholami GH, Panci C, Caffa B. Oocyte donation in menopausal women. *Hum Reprod*. 1993;8:1487.
5. Sauer MV, Paulson RJ, Lobo RA. Pregnancy after age 50: application of oocyte donation to women after natural menopause. *Lancet*. 1993;341:321–3.
6. Sauer MV, Paulson RJ, Lobo RA. Pregnancy in women 50 or more years of age: outcomes of 22 consecutively established pregnancies from oocyte donation. *Fertil Steril*. 1995;64:111–5.

7. Daar JF. Reproductive technologies and the law. Newark: LexisNexis/Matthew Bender; 2005.
8. Faddy MJ, Gosden RG, Gougeon A, Richardson SJ, Nelson JF. Accelerated disappearance of ovarian follicles in mid-life: implications for forecasting menopause. *Hum Reprod*. 1992;7:1342–6.
9. Arias E. United States life tables, 2004. National vital statistics reports. Hyattsville: National Center for Health Statistics; 2007.
10. World Health Organization. The global burden of disease: 2004 update. Geneva: WHO; 2008.
11. Roy A. Specificity of risk factors for depression. *Am J Psychiatry*. 1981;138:959–61.
12. Melhem NM, Walker M, Moritz G, Brent DA. Antecedents and sequelae of sudden parental death in offspring and surviving caregivers. *Arch Pediatr Adolesc Med*. 2008;162:403–10.
13. Salihu HM, Shumpert MN, Slay M, Kirby RS, Alexander GR. Childbearing beyond maternal age 50 and fetal outcomes in the United States. *Obstet Gynecol*. 2003;102:1006–14.
14. Nabukera S, Wingate MS, Alexander GR, Salihu HM. First-time births among women 30 years and older in the United States: patterns and risk of adverse outcomes. *J Reprod Med*. 2006;51:676–82.
15. Human Fertilisation and Embryology Authority. Code of practice. 8th ed. London: Human Fertilization and Embryology Authority; 2009.
16. American Medical Association. Principles of Medical Ethics. American Medical Association; 2001. Available at <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/principles-medical-ethics.shtml>. Accessed April 1, 2010.
17. Centers for Disease Control and Prevention. The burden of chronic diseases and their risk factors: national and state perspectives 2002. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2002.
18. U.S. Department of Health and Human Services: Mental health: a report of the surgeon general—executive summary. Rockville: U. S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Mental Health Services, National Institutes of Health, National Institute of Mental Health; 1999.
19. Unverzagt FW, Gao S, Baiyewu O, Ogunniyi AO, Gureje O, Perkins A, et al. Prevalence of cognitive impairment. *Neurology*. 2001;57:1655–62.
20. Naylor Jr DF, Olson MM. Critical care obstetrics and gynecology. *Crit Care Clin*. 2003;19:127–49.