

Review Article

Is There an Age Limit to Become Pregnant in the Ivf Era?

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Abstract

In the last decade, announcements of births of children conceived by in vitro fertilization (IVF) for women in peri- and postmenopause have multiplied worldwide. Additionally, centers for assistance in human reproduction have received increasing requests from women beyond reproductive age with desire to become pregnant. Is there an age limit to become pregnant in the IVF era? Should we consider the inability to conceive and give birth at advanced reproductive age and in postmenopause a disease? Should we ignore the natural course of human life and the biopsychosocial roles of a mother at different ages? Should assisted reproduction techniques be used as tools to allow women's expression of freedom and their control over reproduction? These and other questions are raised by this contemporary issue, without generally agreed answers. This article will attempt to provide insight for further consideration.

Keywords: IVF; Mother-to-be; Parental age; Medicalization; Regulation of assisted reproduction; Ethics

Introduction

In the last decade, announcements of births of children conceived by in vitro fertilization (IVF) for peri- and postmenopausal women have multiplied worldwide. Additionally, centers for assistance in human reproduction have received increasing requests from women of advanced age with desire to become pregnant, especially in oocyte donation programs. However, while knowledge and practices in the field have advanced, they have been done so without parallel review and discussion amongst society about this paradigm shift. As a result, a belief that motherhood in the 21st century is available beyond natural reproductive limits has been propagated without due rational support.

In this scenario, Brazilian reproductive medicine has been recently regulated by the resolution 2013/2013 of the Federal Board of Medicine, which restricted the use of assisted reproduction techniques (ART) to women with maximum age of 50 years, since the usual risks to maternal and child health have been discarded [1]. However, it is not expected from ethical standards to provide indepth review of biopsychosocial aspects of late motherhood, which will depend on the individualized judgment by the attending physician, according to the protocols from each service.

Is there an age limit to become pregnant in the IVF era? Should we consider the inability to conceive and give birth in peri- and postmenopause a disease? Should we ignore the natural course of human life and the biopsychosocial roles of a mother at different ages? And finally, should ART be used as tools for expression of freedom of women and their control over reproduction? These are current questions without widespread agreement. This article attempts to provide insight for consideration.

The Numbers of Late Motherhood

Lower interest in motherhood and tendency to postpone pregnancy are noted trends in recent decades around the world, in large part resulting from increased female participation in the labor

market and the pursuit of professional development. In the United States, a 50% increase in pregnancies among women with 40 to 44 years of age was documented between 1996 and 2006, mainly involving IVF with younger donor eggs. Additionally, there were 263 pregnancies in women aged between 50 and 54 in 2003 [2-4].

According to the Brazilian Institute of Geography and Statistics – IBGE, and the Information System on Live Births – SINASC, an important behavioral change can be observed in Brazilian women in relation to the number of births at different stages of life [5,6]. Although there is no precise record of births arising from assisted conception in Brazil, it is definitely plausible to consider the influence of advances in reproductive medicine on the numbers over the years. A comparison of births in Brazil by maternal age in 2005 and 2010 shows a relative stabilization in the age group 45 to 49 years (4,002 versus 4,093), but apparently portrays an important increase for women aged 50 and older (57 versus 288 births) [6].

Female Fertility Decline

It is well known that both the quantity and quality of follicles and gametes are inversely related to age, and that a significant proportion of candidates for late motherhood will be infertile when they attempt to conceive. Natural fertility decline can be attributed to numerous causes that may be associated with advancing age, including: decrease in oocyte quality, ovulation inefficiency, sexual dysfunction, evolving uterine or adnexal diseases, endometriosis, genetic factors, smoking or infections. In historical cohorts, rates of infertility among married women in the age groups 20-24, 25-29, 30-34, 35-39 and 40-44 years were 6%, 9%, 15%, 30% and 64 % respectively [7].

A recently published review of natural fertility in ancient populations has demonstrated that the female reproductive potential decreases gradually, but slowly, until an point between 35 and 40 years of age. Thereafter, the reproductive potential declines rapidly, similar to results observed in contemporary populations, even in cases involving intra-uterine insemination and ART [8]. In a recently

published paper, we confirmed the negative interference of age on IVF results. In our study, clinical pregnancy rates of 50.8% were observed for women aged younger than 35 and of 25% for women with 40 or more years. On the other hand, respective pregnancy loss rates were of 18.8% and 37.5% for those same groups [9]. According to the Centers for Disease Control and Prevention, similar rates of births per treatment cycle were observed, declining from 36% for those women under the age of 35 to 4% for those over the age of 42 [10]. Finally, a recent study by Luke and colleagues estimated live birth rates following a third cycle of IVF with non-donor eggs of 63.3% for women under the age of 30, and of 6.6% for those with 43 and older, in an usual perspective [11].

An undeniable fact must be emphasized during patients' counselling process: even modern technologies of assisted reproduction are unable to override the negative interference of time on the natural reproductive potential. Such a reality becomes hard to accept, since modern society is easily seduced by the illusion of eternal youth, stimulated by concepts of dubious evidence, such as those advocated by the so-called anti-aging medicine. A recent study pointed misperceptions of american women aged 40 or more years on the impact of age on fertility. Healthy lifestyle, family history of abundant fertility, incorrect information from friends and doctors, and media reports about pregnancies among celebrities in advanced age led to mistaken beliefs that pregnancy would arrive without difficulty at 40 years of age or that some fertility would be maintained until menopause, around the age of 50 [12].

Pregnancy Beyond Natural Reproductive Age

Does the absence of disease in a woman of 50, 60 or 70 years of age allows us to offer her IVF with donor eggs? Based on confident data from different populations worldwide, definitely the answer must be negative. It is suggested that adult diseases such as diabetes, obesity, cardiovascular problems and breast cancer may result not only from bad living habits or hereditary factors, but also suffer influence from pregnancy physiological aspects, such as high serum levels of steroid hormones. Also IVF itself can determine gestational unfavorable prognosis. When compared to spontaneous pregnancies, IVF pregnancies have been associated with higher rates of obstetric complications such as preeclampsia (odds ratio, OR 1.63, 95% CI 1.53-1.74), placenta previa (OR 2.17, 95% CI 1.74-2.72) and postpartum hemorrhage (OR 1.4, 95% CI 1.38-1.50) [13]; maternal mortality, in turn, may increase by more than twice in pregnancies derived from ART [14].

Pregnancy with Donor Eggs

According to recent studies on IVF pregnancies following egg donation, obstetric complications such as first trimester bleeding [15], preterm birth, low birth weight [16], gestational hypertension [15-17], placenta accreta [18], and postpartum hemorrhage [17] were up to three times more frequent when compared to conventional treatments, with no association with maternal age, all in agreement with previous reports on the subject [19]. Finally, one should also consider the trend of increasing number of transferred embryos in women in their forties; multiple pregnancies resulting from IVF practice can also lead, as known, to complications such as low birth weight and prematurity.

Offspring and Parents' Common Interests: Life Expectancy and Quality of Life

There are additional subjects that should not be ignored when contemplating assisting older couples who want to have children. Involved physicians must consider the consequences not only for the couple but also for the children that may result from their interventions. Do older parents have the same capability to raise and educate children? The question is not easily answered. By the time they reach adolescence and young adulthood, many of the children born to mothers with advanced age will have elder mothers, potential victims of chronic and potentially disabling diseases, including cardiovascular, respiratory, cerebrovascular, diabetes and cancer. Ultimately, while the use of ART should have pregnancy as the ultimate goal, the interests of both parents and the intended offspring must also be taken into account.

According to data from the United Nations, life expectancy at birth in 1960 was approximately 58 years in Brazil, rising to 67.2 in 1995-2000 - slightly below the Latin American average (51.4 to 59.3 years), but above the world average [20]. Considering the trend of annual increases in life expectancy of roughly 4 months, Brazilian children born today to parents aged about 60 are likely to be orphans of father at the age of 12 and of mother at the age of 23.

Additionally, imbalances between long life and healthy living have been observed in populations from several regions around the world. According to a recent systematic analysis for the Global Burden of Disease Study 2010, the evolution paradigm has shifted from premature death to years lived with disability [21]. This information needs to be factored into any discussion about motherhood in postmenopause, even if the surrogate pregnancy is the intended strategy.

Medicalization and Social Iatrogenesis

Foucault has suggested that modern medicine is increasingly taking the management of the body and life of people, thus resulting in guidance not only on health aspects, but also behavioral elements from the fields of sexuality and fertility [22, 23]. Such an appropriation and the exercise of power by medicine over natural stages of human life, and the entrance into fields that until recently belonged to other areas of knowledge had led to a process called medicalization, wherein nonmedical situations are treated as illnesses or disorders [24].

The assignment of the diagnosis of infertility in women beyond natural reproductive age, and particularly postmenopause, is reflected today, by analogy, as a form of medicalization by diagnostic expansion, whereby the natural inability to become pregnant has been transformed into a disease. This process may be referred to as the social iatrogenesis described by Illich [25], by which medicine supports the reproductive inability of women in advanced ages as a disease, and encourages those women to pursue ART as a cure.

Final Considerations

Women over 60 have given birth in several countries in recent years, including Brazil, United States, Italy, Israel and England. However, with the evolution of ART and gamete-donation programs, it is increasingly important to consider whether there is, or should be, an age limit for the IVF mother-to-be. Landau published an article

nearly a decade ago suggesting that the age of 55 should be considered the upper limit for IVF, even though some women of greater age were being treated that time [26]. Today there are certain countries, for example, the Netherlands, where there are regulations that prevent women older than 45 years of age from receiving donor oocytes. This limitation is based on the supposed benefit of the child to be raised by younger parents [27].

Although new reproductive technologies have been widely promoted and utilized, often in support of the autonomy of individuals and with appropriate informed consent, the concerns about the desire for motherhood by women beyond reproductive age are obvious. Certainly pregnancy at an advanced age has not received the deserved attention in a scenario where little is known about its true biopsychosocial and economic burdens related to mothers-to-be and their potential offspring [28].

In spite of the fact that there is currently no laws that regulate assisted reproduction in Brazil, numerous studies on the topic have been published dealing with the legal and ethical perspectives. For example, for Brauner it is clear that the right to gestate is not absolute and thus access to ART must not be unlimited. Brauner justifies his position based on the implied rejection to the rights and interests of the potential child-to-born [29]. In this context, resolution 2013/2013, even if replaced by a future less rigorous normative, encourages the debate in Brazil and therefore stands as a boundary of reproductive medicine practice.

It is recognized that the improvement of ART, especially the development and acquisition of new technologies has led practitioners to use them for the benefit of a greater amount of couples with fertility disorders. However, one should not ignore the fine line that separates the noble mission of helping nature from daring to challenge it. The elements offered in this article hopefully will enrich the reader's views, whether for or against the use of ART at any age. At this time, the goal is to enhance the debate and to provide benefit to reproductive medicine practitioners, infertile couples and their potential offspring.

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