

What should be the upper age limit for reproduction?

The STRAW staging system^[1] describes the various stages of reproductive aging based on ovarian aging. The ovary is probably the only organ in a human being that stops functioning during the lifetime of an individual much before the woman actually dies. The final menstrual period therefore, symbolically and physiologically indicates the end of a woman's capability of reproduction. There are many theories^[2,3] that have tried to describe why menopause takes place and even though none is entirely convincing, menopause is universally accepted as the final nail in the coffin after which a woman cannot reproduce!

It is also very well-known that a normally functioning ovary has profound effects^[4,5] on nearly all organs and systems in the body through the ovarian hormones estrogens and progesterone. As ovarian function declines it affects both reproductive and nonreproductive functions. A woman therefore goes through a major period of physiological readjustment at menopause. And thus, a woman accepts her inability to bear a child when she reaches menopause.

The last century has however witnessed dramatic changes in social behavior, norms, and practices. Women empowerment across the globe has enabled the woman to become more independent in her approach to life. In India as well, women are more educated, get married late, and even think of family building as an obstacle to their careers! Reproduction is thus the last priority for the modern woman. Additionally, phenomenal leaps in scientific advancements and medicine have increased the longevity of mankind. The average age of an Indian woman is now 68 years^[6] and the average age of menopause is 46 years.^[7] Therefore, a woman now lives about 2 decades of her life after menopause and as perimenopause sets in 13 years before,^[1] a woman getting married in her 30s has an already compromised ovarian reserve. Age therefore is a major factor when reproductive function is concerned although some studies have found the oocyte quality is

not very much effected if the woman is under 35^[8,9] even though the quantity of oocytes is less.

The question then is what should be the upper limit for reproduction? If we follow nature and its rules, at least 15 years before the age of menopause—before the endocrinal changes set in.

Contrarily, assisted reproduction has virtually changed the entire approach to reproduction by introducing third party reproduction. Today it is possible for postmenopausal women to become mothers. The oldest mothers were 70 years^[10] when they bore children and many such case reports are found on the internet even though they may not be scientifically reported. Increasing reports of difficulties that these mothers are facing are also found. Rajo Devi who bore a child at age 70, never recovered from the surgery but was still proud to have gone through the pregnancy.^[10]

Even if these stray incidents of complications are ignored keeping in mind the social ostracism that these women undergo because they are barren, the medical fraternity must not forget the findings of the Women's Health Initiative (WHI).^[11] Many couples approach the *in vitro* fertilization (IVF) centers in India today where the common request for IVF is the loss of a child, mainly a male child. Such women are well past their menopause, generally 50+.

The WHI study clearly states that the risk of stroke and other cardiovascular events, breast cancer, and endometrial cancer is increased if hormone replacement treatment (HRT) is given to women well past their menopause.^[11] The recently published^[12] long-term analysis although controversial, still maintains that both estrogens and progestrogens increase the risk of stroke, thromboembolism, and breast cancer. Assisted Reproductive Techniques (ART) entail giving both estrogen and progesterone to these postmenopausal women for prolonged periods. It might be argued that the hormones are not given for long duration, but it is also true that in many patients endometrial preparation may not be adequate first time and many cycles may be tried before an optimal endometrium is formed. Moreover, in many centers it is a practice to carry out mock cycles before the actual treatment cycle in order to get better results.^[12] This definitely means prolonged use of the hormones and even more if the patient becomes pregnant!

There is paucity of IVF data as far as the use of ovarian

Access this article online

Quick Response Code:



Website:

www.jmidlifehealth.org

DOI:

10.4103/0976-7800.122227

hormones is concerned, but attention is now turning towards this as more and more reports of breast cancer are coming in. A recent review on the risk of breast cancer in IVF^[13] does not implicate the process, but advises that more research be done. Moreover, the studies included in this review did not target the elderly population.

Although, the jury is still out on what should the upper limit of age be for reproduction, these medical complications which are debilitating and life-threatening must not be ignored. A recent study on aged men^[14] from 71 to 93 years concluded that high normal levels (34 pg/ml) of estradiol increased the risk of stroke to two-folds, while there was little risk at lower levels. Postmenopausal women also have similar levels of estradiol so it can be extrapolated that older women may behave similarly. Therefore, one must not forget the lesson learnt from the WHI trial and the “window of opportunity” that is available to us. While it may be safe to give hormones after adequate screening to women who are perimenopausal or recently menopausal, the older woman who has been menopausal for more than 5 years, must not be given hormones. Therefore, it may be rational to conclude that women who are otherwise fit and recently menopausal maybe allowed to go through a pregnancy whilst the post postmenopausal women must be refused treatment on medical grounds. There is however, an urgent need to collect and report data on the long-term effects of hormones and outcome of these postmenopausal pregnancies in order to settle this issue.

Sonia Malik

Programme Director, Southend Fertility and IVF Centre,
Delhi National Capital Region, India
E-mail: sm_doc@hotmail.com

REFERENCES

1. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N,

- Utian W, *et al.* Executive summary: Stages of Reproductive Aging Workshop (STRAW). *Fertil Steril* 2001;76:874-8.
2. Rashidi A, Shanley D. Evolution of the menopause: Life histories and mechanisms. *Menopause Int* 2009;15:26-30.
 3. Alvarez HP. Grandmother hypothesis and primate life histories. *Am J Phys Anthropol* 2000;113:435-50.
 4. Dey P, Barros RP, Warner M, Strom A, Gustafsson JA. Insight into the mechanisms of action of estrogen receptor beta. *J Mol Endocrinol* 2013.
 5. Katzenellenbogen BS, Choi I, Delage-Mourroux R, Ediger TR, Martini PG, Montano M, *et al.* Molecular mechanisms of estrogen action: Selective ligands and receptor pharmacology. *J Steroid Biochem Mol Biol* 2000;74:279-85.
 6. Meeta, Digumarti L, Agarwal N, Vaze N, Shah R, Malik S. Clinical practice guidelines on menopause: An executive summary and recommendations. *J Midlife Health* 2013;4:77-106.
 7. Singh M. Early age of natural menopause in India, a biological marker for early preventive health programs. *Climacteric* 2012;15:581-6.
 8. Jansen RP The effect of female age on the likelihood of a live birth from one *in-vitro* fertilization treatment. *Med J Aust* 2003;178:258-61.
 9. Dua M, Malik S, Bhatia V, Prakash V. ART outcome in young women with premature ageing. *J Mid-life Health* 2013;4:230-2.
 10. Available from: http://www.telegraph.co.uk/health/women_shealth/9378142/IVF-the-older-women-who-have-become-mothers.html [Last accessed on 2013, Oct 05].
 11. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, *et al.* Writing Group for the Women’s Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women’s Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33.
 12. Manson JE, Chlebowski RT, Stefanick ML, Aragaki AK, Rossouw JE, Prentice RL, *et al.* Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the women’s health initiative randomized trials. *JAMA* 2013;310:1353-68.
 13. Salhab M, Al Sarakbi W, Mokbel K. *In vitro* fertilization and breast cancer risk: A review. *Int J Fertil Womens Med* 2005;50:259-66.
 14. Abbott RD, Launer LJ, Rodriguez BL, Ross GW, Wilson PW, Masaki KH, *et al.* Serum estradiol and risk of stroke in elderly men. *Neurology* 2007;68:563-8.

How to cite this article: Malik S. What should be the upper age limit for reproduction?. *J Mid-life Health* 2013;4:201-2.