ISAR

FERTILITY PRESERVATION IN YOUNG WOMEN WITH BREAST CANCER

ISAR FERTILITY PRESERVATION SPECIAL INTEREST GROUP

What is the incidence and statistics of breast cancer in the world?

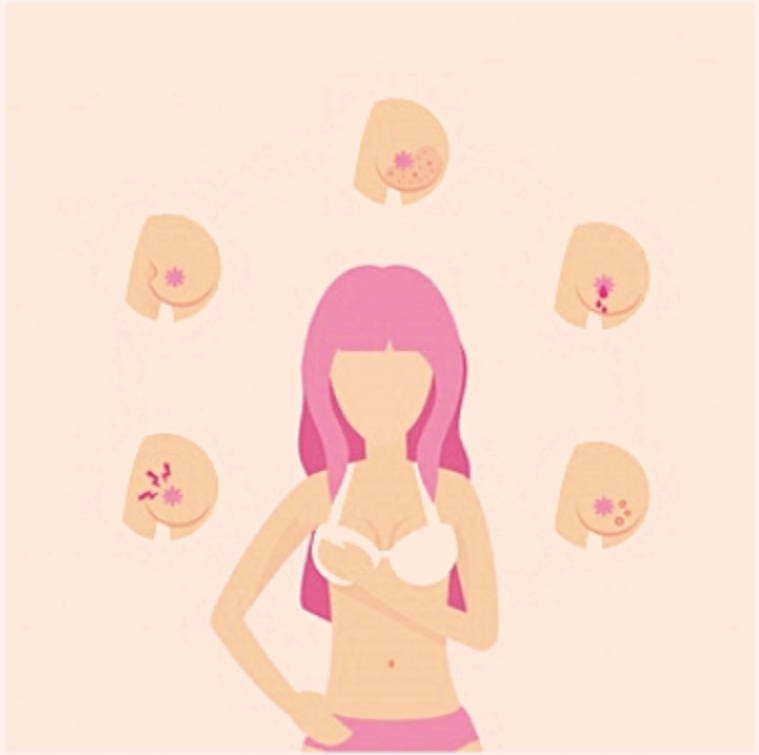
Breast cancer is the commonest cancer in women both in the developed and developing world. Incidence rates vary greatly worldwide from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. In most of the developing regions, the incidence rates are below 40 per 100,000 (GLOBOCAN 2008). The lowest incidence rates are found in most African countries but here breast cancer incidence rates are also increasing.It is estimated that worldwide over 508 000 women died in 2011 due to breast cancer (Global Health Estimates, WHO 2013). Although breast cancer is thought to be a disease of the developed world, almost 50% of breast cancer cases and 58% of deaths occur in less developed countries (GLOBOCAN 2008).

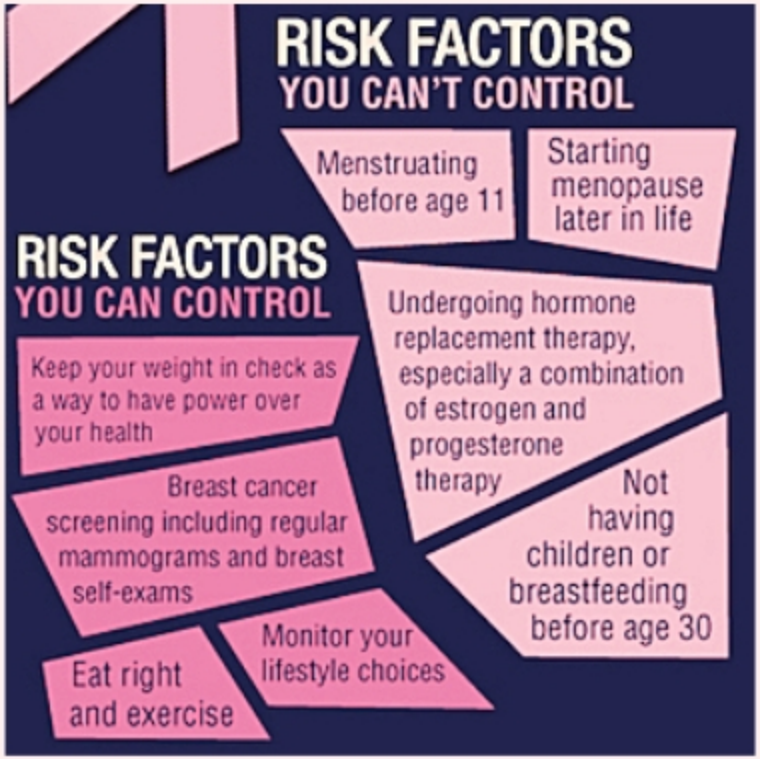
What is the incidence rate of Breast Cancer in India?

Breast cancer has been ranked as number one cancer among Indian females with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women (9, 2017). Indian Council for Medical Research reports 1.5 lakh new breast cancer cases in India, of which 70,000 succumb every year (Feb 5, 2019).

Risk factors for breast cancer :

- ***Prolonged exposure to endogenous estrogens, such as early menarche, late menopause, late age at first childbirth are among the most important risk factors for breast cancer.***
- ***Exogenous hormones - Oral contraceptive and hormone replacement therapy users are at higher risk than non-users.***
- ***Modifiable risk factors- 21% of all breast cancer deaths worldwide is attributable to alcohol use, overweight and obesity, and physical inactivity.***
- ***The increasing adoption of western life-style in low- and middle-income countries is an important determinant in the increase of breast cancer incidence in these countries.***
- ***Breastfeeding has a protective effect (IARC, 2008, Lacey et al., 2009).***





How and whom to counsel and what are the Eligibility criteria for fertility preservation?

As per the 2006 American Society of Clinical Oncology (ASCO) Fertility Preservation Guidelines which was updated in 2013:

- **Every patient in reproductive age group, irrespective of having a partner or not sure about her future child bearing goals should have frank discussions on fertility preservation and her options.**
- **Age is the most important criterion.**
- **Early referral to reproductive specialists.**
- **Addressing fertility preservation as early as possible before starting cancer treatment,**
- **Referring for psychosocial counseling if distress is present and encouraging participation in clinical studies and registries when appropriate.**
- **Interdisciplinary approach should be applied for fertility preservation.**
- **It is the responsibility of the health care team to explain prognosis, treatment options, and potential toxicities and adverse effects of chemotherapy, radiotherapy, and endocrine treatments.**

What are the options for fertility preservation for women with breast cancer?

Looking at the time frame, stage of the disease and age of the patient these are few options for women to freeze their eggs.

- **Ovarian suppression -** by gonadotropin releasing hormone analogues. gonadotropin-releasing hormone (GnRH) agonist has been used concurrently with chemotherapy to prevent premature ovarian failure for young breast cancer patient

- **Oocyte & embryo cryopreservation -** After stimulating the ovaries if patient is in reproductive age group and whether has a partner or not we can make embryos and freeze or do oocyte freezing. Oocyte freezing is no more considered as experimental.

- I**n-vitro maturation**- A technique consisting of retrieval of immature oocytes, which are then matured outside in the laboratory.

- **Ovarian tissue cryopreservation** - In this technique, there is surgical retrieval of ovarian tissue including whole ovarian cortical tissue. Once this ovarian tissue is obtained, it can be used for post-chemotherapy transplantation into the same patient. This tissue can then be stimulated to produce mature or immature oocytes that could be used for producing embryos. This technique is no more considered as experimental, as about more than 100 babies have been born worldwide through this technique.

- **Whole ovary cryopreservation –** This procedure can also be done but it is still in the experimental phase.

What are the challenges in fertility preservation in ER/PR positive or germline mutation positive breast cancer patients?

- Up to 10% of the cases of breast cancer diagnosed in young patients is related to a hereditary condition and, in most of the cases, this is caused by the presence of a germline mutation in the BRCA genes, BRCA1 and BRCA2.

- Patients carrying a deleterious BRCA mutation have an increased lifetime risk of developing breast cancer and other forms of cancer, also, the presence of a BRCA mutation can be associated with impaired ovarian function, meaning that these patients may have an increased risk of fertility-related problems and increased ovarian aging.

- Along with this genetic susceptibility, chemotherapy and radiotherapy adds up its deleterious effect on ovarian function and fertility.

- BRCA positive patients are also prone to develop ovarian cancer so chances for them to undergo prophylactic gynecological surgery at younger age is also high and this can narrow their fertility window.

- Fertility-preserving procedures in BRCA-mutated breast cancer patients are tough but feasible: both oocyte and ovarian tissue cryopreservation are feasible in patients carrying a germline BRCA mutation. But their reproductive potential is lower as compared to non- BRCA mutated patients.

- Same thing is true with ER/PR positive patients, they are susceptible to get the cancers of ovaries and endometrium, they are on long term hormone therapy and have depleted ovarian reserve than other non-ER/PR positive patients.

- Fertility preservation is not that easy but can be done provided they are counselled properly.

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