# CANCERS IN INDIAN WOMEN: AN OVERVIEW

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## Introduction:

India is the most populous country in the world with almost 50% of the population being women. As per the Global Cancer Observatory, GLOBOCAN 2022, our country had 14,13,316 new cancer cases in 2022 with 9,16,827 deaths! Among these, 7,22,138 (>50%) new cases of cancer were women. The number of prevalent cases (5-Yr) of cancer in India was 32,58,518. This is a huge number with a significant burden on our healthcare system. Top three leading cancers in Indian women are, Breast, Cervix uteri and Ovary. Age standardized mortality rate was 62.6 which is fairly high! The key to improve outcomes is to offer Primary prevention as and when possible and early detection by screening for these cancers. We must also ensure accessibility to healthcare to both urban and rural population.

### Statistics at a glance, 2022

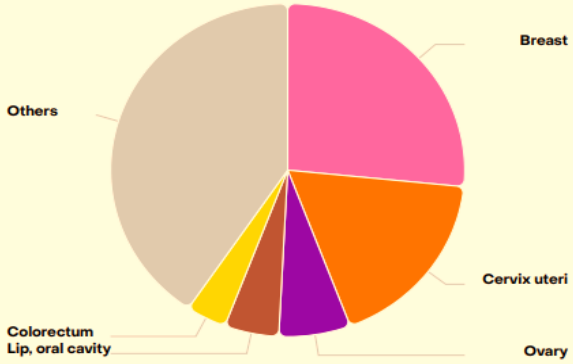
| | Males | Females | Both sexes |
|---|---|---|---|
| Population | 730 746 615 | 675 885 166 | 1 406 631 781 |
| Incidence* | | | |
| Number of new cancer cases | 691 178 | 722 138 | 1 413 316 |
| Age-standardized incidence rate | 97.1 | 100.8 | 98.5 |
| Risk of developing cancer before the age of 75 years (cum. risk %) | 10.6 | 10.7 | 10.6 |
| Top 3 leading cancers (ranked by cases)** | Lip, oral cavity<br>Lung<br>Oesophagus | Breast<br>Cervix uteri<br>Ovary | Breast<br>Lip, oral cavity<br>Cervix uteri |
| Mortality* | | | |
| Number of cancer deaths | 470 055 | 446 772 | 916 827 |
| Age-standardized mortality rate | 66.5 | 62.6 | 64.4 |
| Risk of dying from cancer before the age of 75 years (cum. risk %) | 7.5 | 7.0 | 7.2 |
| Top 3 leading cancers (ranked by deaths)** | Lip, oral cavity<br>Lung<br>Oesophagus | Breast<br>Cervix uteri<br>Ovary | Breast<br>Lip, oral cavity<br>Cervix uteri |
| Prevalence* | | | |
| 5-year prevalent cases | 1 470 047 | 1 788 471 | 3 258 518 |

## Risk Factors for cancer development:

1. **External factors:** Obesity, Sedentary Life-style, Metabolic disorders like Diabetes Mellitus, Tobacco in any form including vaping, e-cigarettes, Alcohol, Infections like HPV, HBsAg, HIV, Environmental pollution
2. Inherent factors: Familial cancers like BRCA 1/2 (BReast CAncer) syndrome. Individual's own susceptibility due to his or her genetic constitution.

### Top 5 Cancers in Indian Women

**Females**




Total: 722 138

| Rank | Cancer site | Number of cases | Percent |
|---|---|---|---|
| 1st | Breast | 192 020 | 26.6% |
| 2nd | Cervix uteri | 127 526 | 17.7% |
| 3rd | Ovary | 47 333 | 6.6% |
| 4th | Lip, oral cavity | 35 947 | 5.0% |
| 5th | Colorectum | 26 678 | 3.7% |
| - | Others | 292 634 | 40.5% |

Number of new cases in 2022, females, all ages

In this overview, five most important cancers in Indian women are discussed. Detailed discussion of management of each cancer is beyond the scope of this article.

## A. Breast Cancer

This is the most common cancer in Indian women as well as in the world. The incidence is 26.6% of all women cancers in India and the mortality rate is 13.7%

- **Signs and symptoms:** Painless lump in breast, Nipple discharge or nipple inversion, Skin changes and systemic symptoms based on metastatic site e.g. bone pain, fracture, breathlessness, headaches, vomiting etc.

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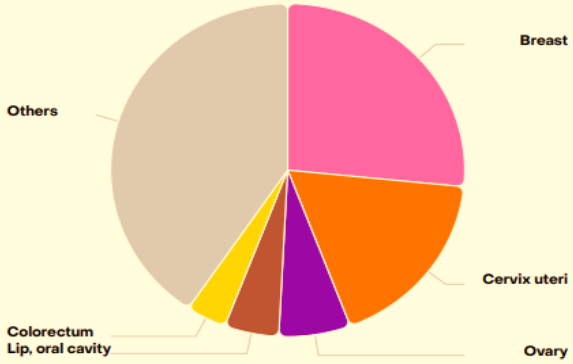


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- **Signs and symptoms:** Painless lump in breast, Nipple discharge or nipple inversion, Skin changes and systemic symptoms based on metastatic site e.g. bone pain, fracture, breathlessness, headaches, vomiting etc.

- **Screening tests:**
  - **Self-Breast examination (SBE):** This can be implemented for all women after the age of 40 years of age so they are able to differentiate between normal and abnormal findings. This practice also keeps women alert about breast cancer. SBE should be done 1 week after menstruation over in premenopausal women or on a fixed date in postmenopausal women every month.
  - **Mammography with Sonography:** Since Indian women present a decade earlier compared to women in western world, annual Mammography should be started from the age of 45 years of age. Simultaneous sonography helps to characterize the lesions found on Mammography. Due to improved Mammography machines, pain during the screening is reduced and radiation exposure is also minimum. Hence, every woman must be motivated to do regular Mammogram till the age of 70 years of age.
  - **MRI Breasts:** MRI can be used in women who have very glandular breasts as Mammography will fail to pick up any lesion. It can be used for women with silicone implant and young women who are BRCA carriers under screening.
- **Principles of management:**

Breast cancer requires a multimodality management involving surgery, radiation and systemic therapy. In today's era, breast conservative surgery is preferred over Modified radical mastectomy. Also, sentinel lymph node biopsy is carried out to decide whether complete axillary dissection is required. Due to this selective approach, incidence of lymphoedema has come down significantly. Radiation techniques have improved drastically giving more precise radiation with minimal toxicities. Short duration radiation protocols are also used in suitable patients.

Systemic therapy involves the Chemotherapy, Hormone therapy, Targeted therapy like Anti-Her2 therapy, Antibody drug conjugates and Immunotherapy. Depending on the stage, Menopausal status and biological nature of the disease, systemic therapy is planned. For Estrogen and/or Progesterone positive tumours, hormone therapy (Tamoxifen, Letrozole, Anastrozole) is an important modality in addition to other modalities. For Her2 positive disease, single or double anti-Her2 agents (Trastuzumab, Pertuzumab) are used. Antibody drug conjugates (ADC) are a novel group of agents where a drug is combined with an antibody with help of a linker. This helps deliver higher doses of anticancer drug intracellularly. Immunotherapy has a role in Triple receptor negative breast cancer. The accessibility and affordability of all the novel agents is still a challenge for Indian women.

## B. Cancer of Uterine cervix (Cervical cancer)

The second most common cancer in Indian women is cervical cancer. The incidence is 17.7% with mortality of 11.2% This is the disease of young women who are in the productive phase of their life.

- **Primary Prevention:** As the majority of cervical cancer cases are related to HPV (Human Papilloma Virus) infection, vaccination against HPV is a very effective strategy to reduce cervical cancer incidence. Ideally, the vaccination should be done before the first sexual exposure. Hence, young girls above the age of 9 years are advised to take HPV vaccines. This has been now recommended as Indian made Vaccine is available. The schedule of administration can vary depending on bivalent or quadrivalent vaccine.
- **Secondary prevention and early detection:** Young women till the age of 25 years are advised to take HPV vaccine as it may still offer benefits. Beyond the age of 25 years, it is individualized and it can still be offered till the age of 45 years. It is important to remember that PAP smear is still required even if a woman has taken the vaccine as about 15% of cervical cancer is caused by non-HPV causes. High performance PAP like HPV DNA PAP is preferable than conventional PAP smears as screening. Even if two HPV DNA PAP smears are done at an interval of 5-10 years, it can bring down the incidence and mortality rate. Every young woman must be motivated to undergo annual gynecologic examination and PAP smear to pick up cervical cancer in early stages.
- **Signs and Symptoms:** Foul smelling per vaginum discharge, bleeding, itching etc. On examination, cervical erosion or a

mass is visible. It bleeds on touch. Hence, biopsy is sometimes risky in such patients.

- **Principles of management:**

Surgery is the treatment of choice for early stage disease, till stage IIa (FIGO). Majority of patients in our country present in locally advanced stage.

Concurrent chemoradiation is the modality of treatment for this stage of the disease. In this treatment, patients receive definitive radiation with weekly injection Cisplatin to make the cells more sensitive to radiation. It is a very effective modality of treatment.

Patients with metastatic disease or recurrent disease, systemic therapy with chemotherapy and Immunotherapy are the standard of care today. Due to non-affordability of Immunotherapy, it is not taken by all our patients. One more targeted agent viz. Injection Bevacizumab anti VEGF Receptor antibody, can be combined with chemotherapy in advanced stage disease. Injection Bevacizumab may lead to bleeding, hypertension, fistula formation. Hence, patient selection is important while planning the management.

## C. Cancer of Ovary, Fallopian tubes and Primary peritoneal cancer

This is the third most common cancer in Indian women with the incidence of 6.6% and mortality of 4.6%

- **Screening and early detection:** Unfortunately, there are no reliable screening tests for ovarian cancer. Tumour marker CA 125 has been promoted as screening test. But it is neither sensitive nor specific for ovarian cancer. Annual pelvic sonography is also not approved as a screening test. Due to the same biological nature, ovarian, fallopian tube and primary peritoneal cancer are treated in the same manner.
- **Signs and Symptoms:** Due to deep seated position of ovarian cancer, majority of patients are diagnosed in late stages. Patients complain of abdominal fullness, bloating, constipation, urinary incontinence or retention, ascites, weight loss, fatigue etc. It requires a high index of suspicion to detect this disease in time.
- **Principles of management:** Surgery and Chemotherapy both are integral part of the management of ovarian cancer. The sequence of the two can differ from case to case. The patients who are eligible for primary debulking surgery with R0 resection are taken up for surgery first followed by chemotherapy. In stage III patients, HIPEC (Hyperthermic Intra Peritoneal Chemotherapy) is offered after achieving R0 status.

If a patient is not fit for primary surgery, patient has a huge ascites or R0 resection cannot be achieved, chemotherapy is started first. After about three to four cycles of chemotherapy, the patient is reassessed for surgery. Interval debulking surgery is planned so as to achieve R0 resection. If R0 resection is not achieved, survival of such patients continues to be poor.

- **Role of maintenance therapy:**

Maintenance therapy is a very important strategy to delay recurrence in ovarian cancer patients as majority of them present in advanced stage. Injection Bevacizumab, anti VEGF (Vascular Endothelial Growth Factor) receptor antibody has been approved for this purpose.

Injection Bevacizumab is started along with chemotherapy and then continued as a single agent for a long time. It is withheld peri-operatively as it can lead to bleeding and delayed healing. It can also lead to hypertension and thrombosis hence patients need to be monitored closely.

As a part of Maintenance strategy, every patient with Ovarian cancer must be tested for Somatic and/or Germline BRCA 1/2 mutations. If a patient is negative for BRCA, Somatic HRD (Homologous Recombination Deficiency) testing must be done. Any patient with either BRCA mutation or HRD positivity, should be considered for PARP (Poly ADP Ribose Polymerase) inhibitors maintenance therapy. These are oral preparations which can be used for a long time. These tablets can lead to fatigue, anaemia, nausea etc. But these are manageable toxicities.

### ****BRCA Syndrome

BRCA 1 and/ or 2 mutations can lead to clinical BRCA syndrome. This involves a very high risk of developing breast, ovarian, pancreatic and prostate (in men but this is

beyond the scope of this article) cancer at an early age. A patient can develop multiple cancers in her life time and may have a strong family history. These women require very close monitoring and screening. The first degree relative of the index case also must be screened thoroughly for BRCA mutations. Clinically, ovarian cancer patient with BRCA mutation, present at an early age, have ascites, high grade serous histology and very good response to Platinum group of chemotherapy.

## D. Other Important Cancers

### Cancer of Endometrium

This malignancy is relatively less common in Indian women with the incidence of 2.5% and mortality of 1%. However, in urban population, there is a gradual increase in number of cases. This is considered as a lifestyle disorder as the risk of this malignancy increases with obesity, sedentary life style and metabolic disorders.

- **Screening and early detection:** There are no reliable screening tests for this disease. Healthy lifestyle like weight control, exercises etc. can help reducing the incidence.
- **Signs and symptoms:** Post menopausal bleeding is the most common presentation. Because of this, the disease is usually detected at an early stage. Patient can also complain of abdominal fullness, bloating etc.
- **Principles of management:**

  The management of endometrial cancer involves surgery, radiation, chemotherapy, Immunotherapy, Targeted therapy and Hormonal therapy.

  For early stage disease, radical surgery with lymph node dissection, omental biopsy is the curative step.

  After surgery, patients with high risk features like high grade tumour, more than half of myometrial invasion, Lympho-vascular space invasion, non-endometroid histology etc. will require radiation to prevent recurrence.

  Patients in stage III and IV, will require chemotherapy as well. Patients with recurrence or metastatic disease will be advised chemotherapy and immunotherapy.

  For low grade histology like well differentiated endometroid carcinoma, hormonal therapy can be tried especially for young women wanting fertility sparing management.
- **Molecular classification of Endometrial carcinoma:**

  Endometrial carcinoma is found to be molecularly heterogenous disease. It is divided into four groups with distinct molecular signature and prognosis.

  - POLE mutated: excellent prognosis
  - Deficient MMR: Moderate prognosis and excellent response to Immunotherapy
  - p53 aberrant: Poor prognosis and moderate response to Chemotherapy
  - NSMP (No Specific Molecular Profile): Moderate prognosis

  This classification has therapeutic implications and prognostic value. For POLE mutated endometrial cancer, de-escalation of therapy can be considered. While for patients with p53 aberrant disease, aggressive approach can be suggested.

### Cancer of Pancreas

As described earlier, BRCA mutated women do have higher incidence of Pancreatic malignancy. Due to lack of this knowledge, this malignancy is not suspected!

Otherwise also, the incidence of this malignancy is gradually increasing in our country due to its association with Diabetes Mellitus. Pancreas is a deep seated organ hence majority of patients are detected in advanced stages.

- **Screening and early detection**: There are no reliable screening tests for this cancer. In families with history of pancreatic cancer and breast, ovarian and prostate cancer, genetic counselling should be done. Germline BRCA and HRD tests should be advised. If a person is found with a pathogenic mutation, close monitoring must be advised.
- **Association of Diabetes and Pancreatic carcinoma:** There is a definite association of between these two clinical conditions. Approximately, one percent of newly diagnosed young diabetic patients will develop pancreatic cancer within three years from the diagnosis. Prediabetic state

is also associated with the same. Acute onset Diabetes prior to diagnosis of pancreatic cancer is thought to be induced by the cancer. With longer duration of Diabetes, the association between Diabetes and pancreatic cancer decreases.

- **Signs and symptoms:** Newly diagnosed Diabetes mellitus (age less than 50 years), Abdominal pain, weight loss, anorexia, Jaundice, backache. High index of suspicion is required to detect this cancer.
- **Principles of management:**

Surgery is the only curative treatment for this disease. The patient may be in resectable, borderline resectable or non-resectable stage.

Chemotherapy is given before surgery in borderline resectable cases so as to convert that patent into a resectable case. Aggressive protocols are used for this purpose in a fit patient.

Chemotherapy will be required after surgery to prevent recurrence and also in advanced stages. For BRCA mutated patients, Platinum based chemotherapy is used due to increased sensitivity to platinum agents in this group of patients.

For patients with metastatic disease, chemotherapy is the main treatment and radiation is used for palliation. These patients are also given Maintenance treatment either with single agent chemotherapy or PARP inhibitors (for BRCA mutated patients)

## Take Home message:

1. Cancer in Indian women is a significant number requiring various preventive and screening strategies. Indian women must be motivated for regular PAP test and Mammograms. HPV vaccine must be given universally to young girls and women as indicated.

2. It is prudent to spread awareness among medical and paramedical fraternity about advances in the management of all these cancers resulting in increased survival in these patients. Value of family history and genetic counselling must be emphasized. High index of suspicion and alertness on the part of medical fraternity can help detect cancers in early stages.

| | New cases | | | | Deaths | | | |
|---|---|---|---|---|---|---|---|---|
| Cancer | Number | Rank | (%) | Cum.risk | Number | Rank | (%) | Cum.risk |
| Breast | 192 020 | 1 | 13.6 | 2.9 | 98 337 | 1 | 10.7 | 1.6 |
| Lip, oral cavity | 143 759 | 2 | 10.2 | 1.1 | 79 979 | 2 | 8.7 | 0.65 |
| Cervix uteri | 127 526 | 3 | 9.0 | 2.0 | 79 906 | 3 | 8.7 | 1.3 |
| Lung | 81 748 | 4 | 5.8 | 0.71 | 75 031 | 4 | 8.2 | 0.65 |
| Oesophagus | 70 637 | 5 | 5.0 | 0.59 | 66 410 | 5 | 7.2 | 0.55 |
| Colorectum | 70 038 | 6 | 5.0 | 0.58 | 40 993 | 7 | 4.5 | 0.33 |
| Stomach | 64 611 | 7 | 4.6 | 0.54 | 57 727 | 6 | 6.3 | 0.49 |
| Leukaemia | 49 883 | 8 | 3.5 | 0.31 | 36 871 | 9 | 4.0 | 0.24 |
| Ovary | 47 333 | 9 | 3.3 | 0.72 | 32 978 | 10 | 3.6 | 0.55 |
| NHL | 39 736 | 10 | 2.8 | 0.31 | 22 972 | 12 | 2.5 | 0.18 |
| Liver | 38 703 | 11 | 2.7 | 0.33 | 36 953 | 8 | 4.0 | 0.31 |
| Prostate | 37 948 | 12 | 2.7 | 0.67 | 18 386 | 14 | 2.0 | 0.29 |
| Larynx | 35 855 | 13 | 2.5 | 0.31 | 22 467 | 13 | 2.5 | 0.21 |
| Brain CNS | 32 574 | 14 | 2.3 | 0.22 | 27 990 | 11 | 3.1 | 0.20 |
| Hypopharynx | 30 510 | 15 | 2.2 | 0.26 | 11 618 | 20 | 1.3 | 0.10 |
| Oropharynx | 23 174 | 16 | 1.6 | 0.19 | 14 202 | 17 | 1.5 | 0.12 |
| Bladder | 22 548 | 17 | 1.6 | 0.19 | 12 353 | 19 | 1.3 | 0.10 |
| Thyroid | 21 873 | 18 | 1.5 | 0.14 | 5 455 | 23 | 0.60 | 0.04 |
| Gallbladder | 21 780 | 19 | 1.5 | 0.18 | 16 407 | 15 | 1.8 | 0.13 |
| Kidney | 17 480 | 20 | 1.2 | 0.14 | 10 464 | 21 | 1.1 | 0.09 |
| Corpus uteri | 17 420 | 21 | 1.2 | 0.30 | 6 845 | 22 | 0.75 | 0.11 |
| Multiple myeloma | 16 526 | 22 | 1.2 | 0.14 | 14 216 | 16 | 1.6 | 0.12 |
| Pancreas | 13 661 | 23 | 0.97 | 0.12 | 12 759 | 18 | 1.4 | 0.11 |
| Penis | 10 443 | 24 | 0.74 | 0.17 | 4 450 | 26 | 0.49 | 0.07 |
| Hodgkin lymphoma | 9 611 | 25 | 0.68 | 0.06 | 3 522 | 27 | 0.38 | 0.02 |
| Salivary glands | 8 107 | 26 | 0.57 | 0.06 | 4 879 | 24 | 0.53 | 0.04 |
| Nasopharynx | 6 519 | 27 | 0.46 | 0.05 | 4 780 | 25 | 0.52 | 0.03 |
| Vagina | 5 000 | 28 | 0.35 | 0.08 | 2 465 | 28 | 0.27 | 0.04 |
| Testis | 4 456 | 29 | 0.32 | 0.05 | 1 050 | 32 | 0.12 | 0.01 |
| Melanoma | 3 689 | 30 | 0.26 | 0.03 | 2 197 | 29 | 0.24 | 0.02 |
| Vulva | 3 112 | 31 | 0.22 | 0.05 | 1 539 | 30 | 0.17 | 0.02 |
| Mesothelioma | 1 613 | 32 | 0.11 | 0.01 | 1 432 | 31 | 0.16 | 0.01 |

3. The government of India and state governments have introduced various schemes for cancer diagnosis and management. Patients in rural and urban areas must have an accessibility to oncology care.

4. Oncology should be included as a part in Medical and paramedical education curricula to make the young medical and paramedical students aware of this Non-communicable disease just like cardiac and metabolic disorders.

5. Last but not the least, documentation of all cancer cases in various registries will help to know the exact number and type of cancers prevalent in Indian patients. This will also help to plan future health policies for our patients.

***Data Source:***

International Agency for Research on Cancer
World Health Organization
GLOBAL CANCER OBSERVATORY