Journal of Comprehensive Clinical Practice
An official Journal of **Vivekananda Polyclinic and Institute of Medical Sciences,** Lucknow, UP, India

REVIEW ARTICLE

Burden of Gynecological Cancers in India

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Abstract

Gynecological cancers contribute to a high epidemiological and economic burden on women and the healthcare system of the country. Breast cancer is the most common cancer in females. Every year there are around five lakh new gynecological cancers worldwide, while more than one lakh of these are diagnosed in India only. Cervical cancer remains the most common gynecological cancer in India. The estimated cancer incidence for the year 2022 is breast (33.0%), cervix (12.3%), ovary (6.5%), and corpus uteri (3.7%) among the top 10 leading sites of cancers in India. Ovarian cancer remains the main cause of cancer-related death in women. The main causes of poor survival are less awareness and late reporting at advanced stages. To overcome the challenge of the rising gynecological cancer burden in India, we need to have accurate data on cancer prevalence and the wider implementation of preventive programs. The prevention, early diagnosis, and treatment of cervical cancer can result in reducing the overall gynecological cancer burden in India.

ARTICLE INFO

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Dates:
Published: 30-12-2023

Keywords:
Cancer burden, Cancer screening, Gynecological cancer, India

Conflict of Interest:
The authors have no conflict of interest

How to Cite:
Parveen N, Gupta B. Burden of Gynecological Cancers in India. Journal of Comprehensive Clinical Practice. 2023;17(2):30-35

Introduction

With the rising trend of cancer, it has become one of the ten leading causes of death in India. Around one in nine people is likely to develop cancer in his/her lifetime in India. The overall estimated cancer incidence in India is around 100.4 per 100,000 population.[1] The Global Cancer Observatory (GLOBOCAN) 2020 report showed that cancer cases in India will increase by 57.5% reaching 2.08 million in 2040 from 2020.[2] The report also showed that India had 678,383 new cases in women and 180,000 (25%) of these cases were gynecological cancers.[3] About one-fifth of women with gynecological cancers belong to the reproductive age group.[4]

The major reasons for the rising trend of gynecological cancers in India are rapid urbanization, sedentary lifestyles, a high proportion of the aging population, pollution, unhealthy diets, malnutrition, tuberculosis, HIV, hepatitis B, hepatitis C, and human papillomavirus (HPV) infection.[5,6] The increasing access to health care facilities especially in urban states of India has also resulted in increased cancer reporting.

The burden of gynecological cancers can be further divided into epidemiological and economic burdens. The various epidemiological parameters are cancer incidence, mortality, and case fatality rate, while the economic parameters involve the economic cost of cancer (direct medical costs, direct nonmedical costs, and indirect costs).

Etiology Of Gynecological Cancers

It is important to discuss the causative factors concerning the gynecological cancer burden. Gynecological cancers comprise cancers of the cervix, ovary,

uterine corpus, fallopian tube, vagina, vulva, and choriocarcinoma. Gynecological cancers are grouped epidemiologically into two categories. The cervical, vulval, and vaginal cancers have certain similarities in that they have a common causative role of human papillomavirus (HPV) infection and they are preceded by long pre-malignant stages, so screening has an important role to reduce the cancer burden. HPV is a sexually transmitted infection and chronic infection with HPV induces pre-malignant changes in epithelial cells which ultimately lead to cancer after many years.[7] Various screening tests e.g., Paps smear, HPV testing, co-testing, and VIA-VILI can be utilized for early identification of Cervical Intraepithelial Neoplasia (CIN).[8] The other co-factors for cancer cervix include high parity, prolonged use of hormonal oral contraceptive methods, multiple sexual partners, smoking, and early age at first sexual contact.[9] The second group of cancers are ovarian, fallopian tube, and corpus cancers which neither have a definite etiology nor have any infective etiology. Most cases of ovarian cancer occur spontaneously, while 10% can have a genetic predisposition.[10] The inherited germline mutations in BRCA-1, BRCA-2 genes, and Lynch type 2 gene can lead to hereditary ovarian cancers. There are many epidemiological risk factors e.g., a family history of ovarian cancer, old age, postmenopausal status, and use of menopause hormone therapy which are associated with causation of epithelial ovarian cancer.[10] The uterine corpus cancer includes mainly endometrial cancer and very rarely uterine sarcoma (leiomyosarcoma). Endometrial cancer is the third most common gynecological cancer in India. It is a hormone-dependent cancer and is associated with risk factors e.g., unopposed estrogen, sedentary lifestyle, and obesity. Routine screening for ovarian and endometrial cancers is not recommended in asymptomatic women.

Estimation Of Gynecological Cancers In India

Cancer registries are made under national cancer control programs.[11] Under the National Cancer Registry Programme (NCRP), the collection of data on various cancers has been performed in India since 1982 by the population-based cancer registries (PBCRs) and hospital-based cancer registries (HBCRs). NCRP works in association with the National Centre for Disease Informatics and Research (NCDIR) of the Indian Council of Medical Research (ICMR), Bengaluru. The main objective of NCRP is to generate accurate data on the prevalence and patterns of various cancers based on data from a part of the population of India. The data is collected retrospectively under population-based cancer registries (PBCR), which takes a significant time and leads to delayed real-time reporting of the most recent cancer statistics. The data from PBCR does not include treatment and outcome parameters of cancers.

On the other hand, hospital-based cancer registries (HBCRs) include data on the treatment and outcomes of the various cancer patients of specific hospitals. Currently, the NCRP of India has a coverage rate of 16.4% of the population (31.6% of urban and 9.5% of the rural population). However, it does not include the data from the two most populous states, Uttar Pradesh and Bihar. There is a need for an expanded coverage rate for cancer registration to strengthen cancer control activities.

The NCRP Report 2020 from 28 Population-Based Cancer Registries (PBCRs) for the years 2012-2016 reported the cancer incidences of various gynecological cancers.[12] Further estimates for the year 2022 on the magnitude and patterns of cancer in India are calculated based on the NCRP Report 2020. By using the age-specific incidence rate for each cancer site, the number of cancer cases for the estimated population was calculated for the year 2022. According to the NCRP Report 2020, the estimated cancer incidence rates for the year 2022 include cancer cervix (12.3%) and ovarian cancer (6.5%), corpus uterine cancer (3.7%) among the top 10 female cancers.[1]

Further, cancer burden measures were calculated as crude rate, Age-Adjusted Rate (AAR), and cumulative risk (probability that an individual will be diagnosed with cancer [0- to 74-years-old age group] in the absence of any competing cause of death and assuming that the current trends prevail over the period) as shown in Table 1.

Table 1: Projected incidence of cancer statistics in India 2022[1]

Site of gynecologic cancer	Patients	Crude rate (CR)	AAR	Cumulative Risk
Cervical cancer	79103	11.9	11.6	1 in 75
Uterine cancer	27922	3.9	4.2	1 in 190
Ovarian cancer	46126	6.5	6.7	1 in 133
Vulval cancer	2258	0.3	0.3	1 in 2454
Vagina & other gynecologic cancer	7961	1.1	1.2	1 in 747

Cervical cancer

Cervical cancer is the most common gynecological cancer in India, contributing one-fifth of the global burden. According to GLOBOCAN 2020, there were 123,907 incident cases and 77,348 deaths in India, with an age-standardized incidence rate of 18 per 100,000 women and a cumulative risk of 2.01%.[2] Around 80% of cervical cancer is diagnosed at an advanced stage, resulting in high mortality.[13] Nearly 60% of cervical cancers are diagnosed at a locally advanced stage and chemo-radiation is the standard of care.[14,15] The prevalence varies from 15 to 55% of all gynecological cancers in different parts of the country. However, according to NCRP 2020, there was an observed significant decrease in the incidence rate of cervical cancer in 10 PBCRs, except in Dibrugarh district and Pune.[12]

Case fatality rates

The data from 11 different population-based cancer registries (PBCR) from India showed that cervical cancer's five-year survival was 51.7%. It ranged from 31.6% in Tripura PBCR to 61.5% in Ahmedabad PBCR. Conversely, in developed countries, where cervical cancer is not as common and case fatality rates are as low as 32%.[16]

Ovarian and adnexal cancers

According to GLOBOCAN 2018, ovarian cancer was the third most common gynecological cancer in India, making up 3.44% (36170) of all cancer cases.[17] There is a documented gradual increase in ovarian cancer over the years based on population-based cancer registries, and it has been reported as the second most common gynecological cancer in India with an estimation of 6.5% for the year 2022.

It is one of the leading causes of gynecological cancer mortality 3.34% (24015) of all cancer deaths in India. Only 15% of ovarian cancers are diagnosed at stage I, which is associated with a 5-year survival rate of 94%. Since, 62% of cases are diagnosed in Stages III and IV, resulting in a 5-year survival rate of 28%.[18] Therefore, it is also called a silent killer. The estimated age-adjusted incidence varies from 0.9 to 8.4 per 100,000 women in India.[19] The incidence of ovarian cancer increases with age. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer have been reported as one group in many studies, though in some studies the latter two cancers have been mentioned as independent sub-groups, comprising 15-20% of cases.[20]

In India, ovarian cancer comes in the top ten cancers in 10 out of 28 Population-based Cancer Registries. There are variations in age-adjusted rates (AARs) among all geographical areas, including North Eastern (NE) states. NE regions have shown higher AARs in the 40 to 44+ age groups, which indicates disease occurrence in lower ages. There has been a steady rise in rates in Bangalore and Bhopal for the years 1984 to 2014. The Hospital-based Cancer Registries showed that 41.9% of patients were diagnosed in the locally advanced stage, followed by 29% of patients with localized, and 29% with distant metastasis.[21]

Uterine corpus cancer

Uterine corpus cancer is more common in developed countries than in developing countries.[26] There have been an estimated 236643 cases worldwide, out of which 113486 (48%) occurred in developing countries for the year 2009.[23] In India 13,328 new endometrial cancer cases were reported with an estimated 5010 deaths in 2018. The age-standardized incidence rate (ASIR) is 2.3/100,000 women.[22,24] Most cases are seen in the 6th and 7th decades of life, with the mean age being 60 years at the time of diagnosis. Uterine sarcomas are rare uterine tumors associated with less favorable outcomes. A study from a regional cancer center in North India reported the median overall survival was 7.67 months (mean 30.19 months),

and 1 to 2-years survival rates were 45.45% and 36.36%, respectively.[25]

Vaginal cancer

Primary vaginal carcinoma is rare and comprises only 1–2% of all malignant gynecological tumors. It is fifth in frequency behind cancer of the uterus, cervix, ovary, and vulva.

Vulvar cancer

It is an uncommon malignancy as per Global Cancer Statistics 2020. It accounts for a 0.2% incidence rate and 0.2% mortality rate in all sites worldwide.[26] In India, vulval cancer ranks 33 in number accounting for 0.26% of new cases and 0.02% of deaths from all sites.[26] The variable pattern of vulvar carcinoma is reported in India. Chhabra *et al.*[27] from Maharashtra reported a decreasing trend of vulvar cancer over 24 years (2.25 to 0.03%), whereas Nandwani *et al.*[28] and Deka *et al.*[29] showed a rising trend over the period.

Choriocarcinoma

Choriocarcinoma (CC) is a malignant neoplasm of trophoblastic tissue that is relatively rare and contributes to less than 1% of all gynecological cancers. The highest incidence was reported in Asia and the lowest in the Americas and Europe. In Asia, 5 to 200 per 100,000 pregnancies have been noted.[30]

Economic Burden Of Gynecological Cancers

The economic burden of gynecological cancers can be further divided into burdens on health systems and patients and their families. The accurate estimation of the real economic burden of gynecological cancers is difficult to assess because of the minimal number of studies. A few Indian studies mentioned the socio-economic impact of cervical cancer.

Maninder et al 2020 calculated the total cost of cervical cancer treatment in 248 patients, including the health system cost and Out of Pocket Expenditure (OOPE) in a public sector hospital in India.[31] The health care cost for various treatment modalities i.e. radiotherapy, brachytherapy, chemotherapy, and surgery was INR 19,494 to 41,388 (USD 291 – 617). The calculated OOPE cost was INR 4,042 to 23,453 (USD 60 – 350), while 62% of patients suffered Catastrophic Health Expenditure (CHE). The high rate of CHE (Odds Ratio: 25.39, *p-value*: <0.001) was seen in the poorest income group.

PK Maurya *et al.*[32] conducted a study on the economic burden of cancer treatment in 474 solid cancer patients (including 152 cervical cancer) in south India. The average out-of-pocket expenditure (OOPE)cost for cancer patients was INR 35,817 (USD 523.6) and INR 20,496 (USD 299.6) for male and female patients, respectively.

Conclusion

Cervical cancer control is very important in reducing the overall gynecological cancer burden in India. There are nearly 59.7 million girls and 272.8 million women in India who are suitable for cervical cancer vaccination and screening, respectively.[33] In 2016, Delhi was the first state where HPV vaccination was started for 11 to 13-year-old age group school girls.[34] Recently, the WHO recommended that women should have at least two HPV tests by the ages of 35 and 45 years.[35] The WHO has set a target of cervical cancer elimination by 2030. In May 2018, the WHO intensified cervical cancer elimination through widespread use of HPV vaccination, screening, early diagnosis, and treatment of pre-cancer and cancer. World Health Assembly (WHA) also initiated a global strategy that includes the following targets:

- 90% of girls should be vaccinated with two doses of HPV vaccine by 15 years of age;
- 70% of women should undergo screening at 35 and 45 years of age; and,
- 90% of women with pre-cancer and cervix cancer should be treated to achieve a goal of <4 cases per 100,000 women.

To overcome the challenge of the growing burden of gynecological cancers in India, we need to have accurate data on cancer and wider implementation of preventive programs for the early detection of cancer both in urban and rural areas. The establishment of population-based cancer registries should be prioritized to cover more populations.

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