

## RESEARCH ARTICLE

# Pattern of Reproductive Cancers in India

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### Abstract

**Background:** Reproductive cancers are those that affect the human organs that are involved in producing offspring. An attempt is made in the present communication to assess the magnitude and pattern of reproductive cancers, including their treatment modalities, in India. The cancer incidence data related to reproductive cancers collected by five population-based urban registries, namely Bangalore, Bhopal, Chennai, Delhi and Mumbai, for the years 2006-08 were utilized. The reproductive cancers among females constituted around 25% of the total and around 9% among males. Among females, the three major contributors were cervix (55.5%), ovary (26.1%) and corpus uteri (12.4%). Similarly among males, the three major contributors were prostate (77.6%), penis (11.6%) and testis (10.5%). For females, the AAR of reproductive cancers varied between 30.5 in the registry of Mumbai to 37.3 in the registry of Delhi. In males, it ranged between 6.5 in the registry of Bhopal to 14.7 in the registry of Delhi. For both males and females, the individual reproductive cancer sites showed increasing trends with age. The leading treatment provided was: radio-therapy in combination with chemo-therapy for cancers of cervix (48.3%) and vagina (43.9%); surgery in combination with chemo-therapy (54.9%) for ovarian cancer; and surgery in combination with radio-therapy for the cancers of the corpus uteri (39.8%). In males, the leading treatment provided was hormone-therapy for prostate cancer (39.6%), surgery for penile cancer (81.3%) and surgery in combination with chemo-therapy for cancer of the testis (57.6%)

**Keywords:** Reproductive cancers - cervix - ovary - corpus uteri - prostate - penis - testis

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### Introduction

Cervix and Ovarian cancers are the two leading sites of cancer among women in India. Based on the data of 13 Population Based Cancer Registries in India, Cervix and Ovarian cancer are the second and the fourth most common cancer in India, NCRP (2013). The cancer of the Corpus uteri has also shown an emerging trend over the years Takiar and Vijay (2010). Similarly, among men, Prostate cancer has shown an emerging trend Takiar and Vijay (2011). All these sites belong to Reproductive sites of cancers. Reproductive cancers are those that affect the human organs that are involved in producing offspring. In India, while there are studies (Murthy et al., 2005, Takiar and Srivastav 2008; Yeole, 2008; Nandakumar et al., 2009; Takiar and Vijay, 2010; 2011) available related to one or more sites of cancers that are associated with reproductive cancers, hardly there is any study discussing all the sites of cancers together related to reproductive cancers. An attempt is therefore made in the present communication to assess the magnitude and pattern of reproductive cancers including their treatment modalities in India.

### Materials and Methods

The cancer incidence data related to reproductive

cancers collected by five urban registries namely Bangalore, Bhopal, Chennai, Delhi and Mumbai for the years 2006-08 were utilized. In women, the sites which are included under reproductive cancers with respective ICD10 codes are: Vulva (C51), Vagina (C52), Cervical Uteri (C53), Corpus Uteri (C54), Uterus Unspecified (C55), Ovary etc. (C56), Other Female genital (C57) and Cancers of Placenta (C58). In men, it include Penis (C60), Prostate (C61), Testis (C62) and Other Male Genital (C63) NCRP 2013.

#### *Percentage contribution of reproductive sites*

All cancer cases of individual reproductive sites when added will give the total number of reproductive cancers. When this number is expressed as percentage of all cancers, provides an idea about their percentage contribution to all cancers. In order to decide the major sites of reproductive cancers, the number of cancer cases by individual reproductive site is expressed as the percentage of total number of reproductive cancers. If 'n' represents the number of reproductive cancers and 'x' represents the number of cases by an individual reproductive cancer site (S) then  $(x/n) \times 100$  provides the percentage contribution of site 'S' to total reproductive cancers.

To form an idea about the burden of the Reproductive

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cancers in India, it is necessary to study their Crude Rates. Crude Rate (CR): The Crude Rate is obtained by the division of number of cases by the corresponding estimated population (midyear) for given reproductive site, sex, area and year (period) and multiplied by 100000. In terms of formula it is given by:  $CR = \frac{\text{New cases of cancer for a given site and year or period}}{\text{Estimated mid-population of the same year or period}} \times 100000$

**Age specific rate (ASR)**

Cancer incidence is known to increase with age. Hence, it is important to assess the Age Specific Rates. It is obtained by the division of the total number of cancer cases of a given site by the corresponding estimated midyear population for given age, sex, period and multiplying by 100000.

$ASR = \frac{\text{New cancer cases of a site in the given age group, sex and year (period)}}{\text{Estimated mid-population of the same year (period) for given age group and sex}} \times 100000$

**Age adjusted rate (AAR)**

In order to make the rates comparable between developed and developing countries, an Age Adjusted Rate is derived using a common world standard population proportions as weightings to various age specific rates. The details of it can be seen in the report NCRP 2010. The formula for derivation of AAR is given below:  $AAR = \frac{\sum(a_i \times w_i)}{\sum w_i} \times 100000$  for all  $i=1,2,3, \dots, 16$ . Where:  $a_i$  = Age specific rate for  $i^{th}$  age group and;  $w_i$  = World standard population for  $i^{th}$  age group. Note that  $i=1$  refers to 0-4 age group;  $i=2$  refers to 5-9 age group and so on.

Treatment modalities for Reproductive cancers: Hospital Based Cancer Registries (HBCR) working under the co-ordination of National Cancer Registry Programme (NCRP) are routinely collecting information on treatments provided to all cancer patients. Same information was utilized to throw light on the treatment modalities carried out for reproductive cancers in India.

**Results**

The five registries reported 47054 cases of cancers during the period 2006-08 (NCRP 2010), out of which 12044 (25.6%) cases constituted that of reproductive cancers. In case of females, the percentage of reproductive cancers varied from 24.3% in the registry of Mumbai to 28.1% in the registry of Bhopal. While, for males, the percentage of reproductive cancers varied from 5.4% in the registry of Bhopal to 9.0% in the registry of Bangalore (Table 1).

Among reproductive cancers for females, the three major contributors are: Cervix (55.5%), Ovary (26.1%) and Corpus uteri (12.4%). Each of the other sites, in general, contributed less than 3% of the total reproductive cancer cases (Table 2).

Among reproductive cancers in males, the three major contributors are: Prostate (77.6%), Penis (11.6%) and Testis (10.5%). Other male genital cases contributed only 0.3% of the total reproductive cancer cases (Table 3).

For females, the CR of reproductive cancers varied

between 22.0 in the registry of Bhopal to 29.6 in the registry of Chennai. While, in the case of AAR, it varied between 30.5 in the registry of Mumbai to 37.3 in the registry of Delhi. In males, the CR (AAR) ranged between 4.0 (6.5) in the registry of Bhopal to 7.6(14.7) in the registry of Delhi (Table 4).

The Age Specific Rates of Reproductive cancer sites for females, pooled for all selected five urban registries, is shown in Table 5. The cervix incidence rate starts increasing rapidly after the age of 35 years and reaches to

**Table 1. Number and Percentage of Reproductive Cancers by Sex and Selected Urban Registries of India**

| Cancer Registry | Females                   |             |                  | Males                     |             |                  |
|-----------------|---------------------------|-------------|------------------|---------------------------|-------------|------------------|
|                 | Reproductive Cancer cases | All cancers | % of all cancers | Reproductive Cancer cases | All cancers | % of all cancers |
| Bangalore       | 1910                      | 7210        | 26.5             | 522                       | 5812        | 9.0              |
| Bhopal          | 546                       | 1946        | 28.1             | 108                       | 1992        | 5.4              |
| Chennai         | 1996                      | 7866        | 25.4             | 428                       | 7392        | 5.8              |
| Delhi           | 3364                      | 12602       | 26.7             | 1182                      | 13708       | 8.6              |
| Mumbai          | 4228                      | 17430       | 24.3             | 1281                      | 15602       | 8.2              |
| Pooled          | 12044                     | 47054       | 25.6             | 3521                      | 44506       | 7.8              |

\*Source: National Cancer Registry Programme (2010): Three-year Report of Population Based Cancer Registries (2006-2008)

**Table 2. Reproductive Cancers Sites and their Percentage Contribution to Total Reproductive Cancers-Females**

| Cancer Site          | Bangalore | Bhopal | Chennai | Delhi | Mumbai | Pooled |
|----------------------|-----------|--------|---------|-------|--------|--------|
| Cervix uteri         | 57.2      | 62.3   | 59.4    | 54.5  | 52.8   | 55.5   |
| Ovary                | 21.8      | 26.0   | 24.0    | 28.4  | 27.3   | 26.1   |
| Corpus uteri         | 14.3      | 9.0    | 9.7     | 12.1  | 13.4   | 12.4   |
| Uterus unspecified   | 2.7       | 0.4    | 2.0     | 2.1   | 2.7    | 2.3    |
| Vagina               | 2.1       | 0.5    | 3.2     | 1.2   | 2.2    | 2.0    |
| Vulva                | 1.8       | 0.5    | 1.5     | 1.2   | 1.3    | 1.3    |
| Placenta             | 0.1       | 1.3    | 0.2     | 0.2   | 0.1    | 0.2    |
| Other Female genital | 0.1       | 0.0    | 0.1     | 0.2   | 0.2    | 0.1    |

| Reproductive cancer cases - |      |     |      |      |      |       |
|-----------------------------|------|-----|------|------|------|-------|
| Total                       | 1910 | 546 | 1996 | 3364 | 4228 | 12044 |

**Table 3. Reproductive Cancers Sites and their Percentage Contribution to Total Reproductive Cancers-Males**

| Cancer Site        | Bangalore | Bhopal | Chennai | Delhi | Mumbai | Pooled |
|--------------------|-----------|--------|---------|-------|--------|--------|
| Prostate           | 77.0      | 75.0   | 66.4    | 81.4  | 78.5   | 77.6   |
| Penis              | 13.0      | 8.3    | 22.2    | 9.1   | 10.0   | 11.6   |
| Testis             | 9.8       | 16.7   | 11.4    | 9.5   | 10.9   | 10.5   |
| Other Male genital | 0.2       | 0.0    | 0.0     | 0.1   | 0.6    | 0.3    |

| Reproductive cases |     |     |     |      |      |      |
|--------------------|-----|-----|-----|------|------|------|
| Total              | 522 | 108 | 428 | 1182 | 1281 | 3521 |

**Table 4. Crude Rate (CR) and Age Adjusted Rate (AAR) per 100000 Person of Reproductive cancers by Sex and Selected Urban Registries of India**

| Registry  | Females   |           | Males   |          |
|-----------|-----------|-----------|---------|----------|
|           | CR        | AAR       | CR      | AAR      |
| Bangalore | 27.9      | 36.3      | 6.9     | 11.0     |
| Bhopal    | 22.0      | 31.2      | 4.0     | 6.5      |
| Chennai   | 29.6      | 32.9      | 6.2     | 7.2      |
| Delhi     | 25.4      | 37.3      | 7.6     | 14.7     |
| Mumbai    | 25.3      | 30.5      | 6.3     | 10.7     |
| Range     | 22.0-29.6 | 30.5-37.3 | 4.0-7.6 | 6.5-14.7 |
| Mean      | 26.0      | 33.6      | 6.2     | 10.0     |
| SD        | 2.89      | 3.03      | 1.35    | 3.30     |

it peak in the age group of 55-64 years. Similar trend was also seen in the case of corpus uteri and ovarian cancer. In general, the Age Specific Rate (ASR) for reproductive cancers increased rapidly with advancement of every 10 years after the age of 25 years. It starts from 0.9 for the age group below 25 years to 131.0 in 55+ years age group. In males the ASR of prostate cancer increases rapidly particularly after the age of 55 years and reaches to its peak after the age of 65 years (Table 6). For both males and females, the Individual reproductive cancer sites showed the increasing trend with age.

The type of treatment provided to female cancer patients according to their reproductive cancer sites is shown in Table 7. The leading treatment provided was Radio-therapy in combination with Chemo-therapy for the cancers of Cervix (48.3%) and Vagina (43.9%); Surgery in combination with Chemo-therapy (54.9%) for the cancer of Ovary; Surgery in combination with Radio-therapy for the cancers of Corpus uteri (39.8%) and Uterus unspecified (36.7%); Surgery for the cancer of Vulva (34.1%) and Chemo-therapy for the cancer of Placenta (85.7%).

The type of treatment provided to male cancer patients according to their reproductive cancer sites is shown in Table 8. The leading treatment provided was Hormone-therapy for Prostate cancer (39.6%); Surgery for penile cancer (81.3%); Surgery in combination with Chemo-therapy for cancer of testis (57.6%).

**Table 5. Age Specific Rate (ASR) per 100000 person of Reproductive Cancer sites-Females-Pooled (2006-2008)**

| Site of Cancer        | <25 | 25-34 | 35-44 | 45-54 | 55-64 | 65+   |
|-----------------------|-----|-------|-------|-------|-------|-------|
| Cervix Uteri          | 0.1 | 3.2   | 20.2  | 48.7  | 69.8  | 61.9  |
| Corpus Uteri          | 0.0 | 0.4   | 2.4   | 8.8   | 22.6  | 17.6  |
| Ovary                 | 0.8 | 2.9   | 7.4   | 19.5  | 31.6  | 30.3  |
| Other female genitals | 0.0 | 0.4   | 1.2   | 3.9   | 7.5   | 11.7  |
| Pooled                | 0.9 | 6.8   | 31.2  | 80.9  | 131.5 | 121.5 |

**Table 6. Age Specific Rate (ASR) per 100000 person of Reproductive cancer sites-Males-Pooled (2006-2008)**

| Site of Cancer      | <25 | 25-34 | 35-44 | 45-54 | 55-64 | 65+   |
|---------------------|-----|-------|-------|-------|-------|-------|
| Prostate            | 0.0 | 0.0   | 0.2   | 2.3   | 20.1  | 101.8 |
| Penis               | 0.0 | 0.2   | 0.7   | 1.8   | 3.8   | 6.6   |
| Other male genitals | 0.4 | 1.3   | 0.9   | 0.6   | 0.8   | 1.3   |
| Pooled              | 0.4 | 1.5   | 1.8   | 4.8   | 24.7  | 109.7 |

**Table 7. The distribution of Treatment by Different Reproductive Cancer Sites-Females**

| Treatment          | Cervix Uteri | Ovary | Corpus Uteri | Vagina | Vulva | Placenta | Uterus unspecified |
|--------------------|--------------|-------|--------------|--------|-------|----------|--------------------|
| Radio therapy (R)  | 39.2         | 0.5   | 5.9          | 39.5   | 18.8  | 0.0      | 6.7                |
| Chemo therapy (C)  | 2.3          | 33.1  | 3.5          | 7.8    | 15.3  | 85.7     | 10.0               |
| Surgery (S)        | 3.3          | 8.7   | 32.0         | 2.4    | 34.1  | 2.0      | 10.0               |
| R+C                | 48.3         | 1.1   | 2.8          | 43.9   | 9.4   | 2.0      | 0.0                |
| R+S                | 3.3          | 0.5   | 39.8         | 1.0    | 3.5   | 0.0      | 36.7               |
| C+S                | 0.6          | 54.9  | 5.8          | 1.5    | 12.9  | 6.1      | 23.3               |
| S+R+C              | 2.9          | 0.5   | 8.6          | 2.9    | 4.7   | 4.1      | 13.3               |
| Other combinations | 0.1          | 0.7   | 1.6          | 1.0    | 1.3   | 0.1      | 0.0                |
| Number             | 5604         | 1464  | 538          | 205    | 85    | 49.0     | 30                 |

\*Based on Pooled HBCR data of Bangalore, Chennai, Mumbai, Thiruvananthapuram, Dibrugarh (2004-06)

## Discussion

The data has shown that among females, about 25% of the total cancers constitutes that of reproductive cancers while among males its percentage is around 8%. In females, the leading three sites of reproductive cancers are Cervix, Ovary and Corpus uteri. In males, they are Prostate, Penis and Testis. These leading sites contributed more than 90% of the total reproductive cancers. The data has shown that the age specific rates in women above 55 years increases to almost 4 folds as compared to that seen in 35-44 years age group of women. In men, above 55 years age, the rise was found to be 5 to 20 times higher as compared to that seen in 35-44 years age group. Thus, like any other cancer, the age specific rates of reproductive cancers show an increasing trend.

There were an estimated 530000 cases of cervical cancer and 275000 deaths from the disease in 2008. Cervical cancer is generally caused by sexually acquired infection with certain types of HPV; Schiffman M, Solomon D (2013). Two HPV types (16 and 18), almost cause 70% of cervical cancers and precancerous cervical lesions WHO (2013). Sexual activity that increases the risk for infection for cervical cancer includes: Having multiple sexual partners or Sexual intercourse at a young age (WHO 2013, Reproductivecancer.com). Regular screening via Pap Smears greatly reduces the risk for developing invasive cervical cancer by detecting precancerous changes in cervical cells. Women who do not receive regular Pap smears have a higher risk for

**Table 8 The Distribution of Treatment by Different Reproductive Cancer Sites-Males**

| Treatment           | Prostate | Penis | Testis |
|---------------------|----------|-------|--------|
| Radio therapy (R)   | 10.2     | 0.9   | 0.0    |
| Chemo therapy (C)   | 2.0      | 4.7   | 21.2   |
| Hormone therapy (H) | 39.6     | 0.0   | 0.0    |
| Surgery (S)         | 8.6      | 81.3  | 12.4   |
| R+H                 | 20.1     | 0.0   | 0.0    |
| R+S                 | 1.2      | 4.4   | 4.7    |
| H+S                 | 3.5      | 0.0   | 0.0    |
| S+C                 | 0.0      | 7.0   | 57.6   |
| S+R+C               | 1.8      | 1.6   | 2.9    |
| Other combinations  | 13.0     | 0.1   | 1.2    |
| Number              | 512      | 316   | 170    |

\*Based on Pooled HBCR data of Bangalore, Chennai, Mumbai, Thiruvananthapuram, Dibrugarh (2004-06)

the condition (WHO 2013, Reproductivecancer.com, Office of Population Affairs). The early stages of cervical cancer may be completely symptom free. The possible symptoms in early stages may include: Vaginal bleeding; contact bleeding; moderate pain during sexual intercourse; vaginal discharge. The symptoms of advanced cervical cancer may include: loss of appetite; weight loss; fatigue; pelvic pain; single swollen leg; heavy bleeding from the vagina (WHO 2013, Reproductivecancer.com, Office of Population Affairs).

Ovarian cancer is the fourth most common cancer among women in India. Based on the data of Mumbai PBCR, the AAR of death rate in ovarian cancer was 3.7 as compared to AAR of 3.9 seen in cervix cancer NCRP (2010). For ovarian cancer, the risk factors are: Family history of ovarian cancer; Fertility Drugs; Hormone replacement therapy (HRT) with estrogens only (without progesterone); Late menopause (after age 52); Never given birth or delivering first child after the age 30 (Reproductivecancer.com, Office of Population Affairs). The symptoms that are often found to be associated with ovarian cancer are: Loss of appetite, full feeling, Unexplained weight gain, Swelling and Pain in the lower abdomen, Lower back pain, Abnormal vaginal bleeding and Pain during sex (Reproductivecancer.com, Office of Population Affairs, Can Teen).

For cancer of corpus uteri, the risk factors are: Exposure to estrogen increases the risk for developing the disease and estrogen often affects tumor growth. The following factors increase estrogen exposure: Early menarche (before the age 12 years), Hormone replacement therapy (HRT) with estrogens only (without progesterone); Late menopause (after age 52); Never given birth or delivering first child after the age 30 (Reproductivecancer.com, Can Teen). The symptoms that are often found to be associated with Abnormal uterine bleeding, abnormal menstrual periods, Bleeding between normal periods in premenopausal women, vaginal bleeding and/or spotting in postmenopausal women, Lower abdominal pain and Anemia caused by chronic loss of blood (Reproductivecancer.com, Office of Population Affairs, Can Teen).

In men, Prostate cancer constitutes about 80% of newly diagnosed reproductive cancer cases. The risk for developing prostate cancer rises significantly with age. It's AAR increases rapidly after the age of 55 years (20.1) and reaches to its peak (101.8). It has been found to be an emerging cancer in India Takiar and Vijay (2011). A family history of prostate cancer increases the risk (Reproductivecancer.com, Office of Population Affairs, Can Teen). Other possible risk factors include: Diet high in saturated fat, Sedentary lifestyle and Smoking. Early prostate cancer usually causes no symptoms. However there are some symptoms and they are: frequent urination, increased urination at night, difficulty starting and maintaining a steady stream of urine, blood in the urine, and painful urination, problems with sexual function(Reproductivecancer.com, Office of Population Affairs, Can Teen).

The main risk factor for testicular cancer is a problem called undescended testicle(s) and accounts for 10% of the

cases. A family history of prostate cancer increases the risk. Other possible risk factors include: HIV infection, Cancer of the other testicle, Body Size(Reproductivecancer.com, Can Teen). Symptoms may include one or more of the following: a lump in one testis or a hardening of one of the testicles, pain and tenderness in the testicles, loss of sexual activity, build-up of fluid in the scrotum, a dull ache in the lower abdomen or groin, an increase, or significant decrease, in the size of one testis, blood in semen(Office of Population Affairs, Can Teen). Possible signs of penile cancer include sores, discharge, and bleeding. The risk factors include: Being age 60 or older. Having phimosis (a condition in which the foreskin of the penis cannot be pulled back over the glans), Having poor personal hygiene, Having many sexual partners, Using tobacco products ( Office of Population Affairs).

For cancer patients in PBCRs, the detailed information on treatment is not available. Therefore, the HBCR data (2009) was utilized to throw light on treatment details. The treatment depends on the type of cancer. Reproductive cancers are often treated with Chemotherapy (medicine to kill cancer cells), Hormone therapy (medicine to block hormones that are related to cancer growth) or Radiation. Depending on the type of cancer, one or more treatments may be used together. Radiotherapy alone or in combination with Chemo-therapy was the preferred choice of treatment in the cancers of Cervix uteri and Vagina. Surgery alone or surgery in combination with Radio-therapy was the preferred choice of treatment in the cancers of Corpus uteri and in cancers of Uterus unspecified. In the case of cancers of Ovary or Placenta, the preferred choice of treatment was essentially Chemo-therapy or Chemo-therapy in combination with Surgery. In case of men, for Prostate cancer, the preferred choice of treatment was mainly Hormone therapy while it was Surgery for Penile cancer. In case of Cancer of Testis, Chemo-therapy or Chemo-therapy in combination with Surgery was the main course of treatment.

Survival rates are important for prognosis, for example whether a type of cancer has a good or bad prognosis can be determined from its survival rate. Cervix cancer is considered as one of the major leading sites among females. Survival studies carried out in India (IARC, 2011) have shown that the 5 years absolute % survival for Cervix cancer is around 42% while for Ovarian cancer it is relatively less and is around 23%. Among males, Prostate cancer has the least absolute % survival of 24% while Penile cancer (43.6%) and Testicular cancer (53.0%) have relatively higher 5 years absolute % survivals.

It is to remember that an early diagnosis leading to an early treatment can increase the chances of survival significantly among the Reproductive cancer cases. The success of early detection and cancer treatment may be measured by improvement in survival from cancer.

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