

“Emerging Trends in Epidemiology of Breast, Prostate and Gall bladder cancer”

Girish Sharma^{1,2}, Sumedha Sharma^{2*}, Prerna Sehgal^{2*}

¹Amity Center for Cancer Epidemiology and Cancer Research, and

²Amity Institute of Biotechnology, Amity University Uttar Pradesh,
NOIDA (UP), India.

Email: sharmagi03@gmail.com

Phone: +91(0)-120-4391522;

ABSTRACT

Being the second most common disease after cardiovascular disorders, cancer has come to be known as one of the leading causes of death. Almost 14.1 million people were diagnosed in 2012 and the world cancer burden has been expected to increase in the subsequent years. In 2012, Breast cancer has secured the top most position for causing maximum number of deaths among females. Almost 12% of worldwide cancer burden is because of breast cancer. It has become one of the major threats around the world. Furthermore, Prostate cancer, though, a disease of the elderly, has slowly inched its way to become the second most likely cancer to be diagnosed in men. One of the cancers, that require special attention, is Gall Bladder Cancer. Due to pitiful prognosis, it is diagnosed at a very late stage and is thus, responsible for high mortality rates throughout the world. In this study, we have focused on updates of global incidence, mortality and 5-year prevalence of Breast, Prostate and Gall Bladder Cancer. Emphasis is also given on recent updates in context of Indian scenario. Additionally, we have mentioned the signs and symptoms and various risk factors associated with them to comprehend their etiology, as well as mode of diagnosis and treatment options available.

Key Words: Epidemiology, Risk Factors, Breast Cancer, Prostate cancer, Gall bladder cancer.

INTRODUCTION

In order to understand the reason for prevalence of a certain cancer in a particular population various parameters need to be taken into account. Also, it is necessary to understand the signs and symptoms and to carry out epidemiological studies. These studies give an outlook of the number of causes and risk factors responsible for a specific cancer. This can help in designing various treatment options that can be customized. Therefore, these facts and figures of cancer are the best way of assessing the situation of the cancer burden globally, it gives the idea on how the world is coping up with breast, prostate and gall bladder cancer and what can be predicted for the future.

Cancer is represented by a group of diseases pertaining to abnormal cellular proliferation. It is one of the leading causes of death in the world. According to *GLOBOCAN 2008*, 12.7 million people were diagnosed with cancer globally and out of these, 7.6 million died [1]. By the year 2012, this number got increased to 14.1 million new cancer cases and 8.2 million cancer-related deaths [11]. Also, around 32.6 million people alive, over the age of 15 years, were diagnosed with cancer in the five-year prevalence period 2008-2012. Here, we provide the comprehensive overview of cancer incidence, mortality, and 5-year prevalence of Breast, Prostate and Gall Bladder Cancer both globally and in context of Indian population (Table 1) by using the recent population-based data available [11].

In 2012, Breast cancer became the largest cancer among women globally. Its incidences have increased by more than 20%, while mortality rate has increased by 14%. These numbers are expected to increase subsequently over the years. On the other hand, Prostate cancer has been the second most commonly diagnosed cancer among men and the fifth leading cause of death from cancer in men [6]. Prostate cancer is mainly a disease of the elderly men and most of the cases occur in men aged 65 years and above.

Surprisingly, though Gall Bladder Cancer (GBC) is a rare malignancy which involves insidious onset, rapid local invasion and progression, but has shown very high mortality rates in regions where it is prevalent. It is the fifth most common gastrointestinal (GI) malignancy following colon, pancreas, stomach and oesophagus. Gallbladder carcinoma has been known to be two to six times more common in women than in men [12].

MATERIALS AND METHODS

Incidence and mortality data

This study focuses on worldwide mortality and incidence data from 2008 to 2012. Data collection was done from various sources viz. GLOBOCAN 2008 [an initiative of International Agency for Research on Cancer (IARC)], GLOBOCAN 2012 [10, 11], Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute (NCI) [24] etc. Furthermore, we have reviewed various epidemiological studies conducted on the above mentioned cancers.

BREAST CANCER

The increasing trends of breast cancer, in both developed and developing countries, are an actual threat. A lot of effort is required for determining accurate diagnosis, prognosis and treatment aspects to decrease the rate of breast cancer. It is the second most common cancer in the world. In 2012, globally around 1.67 million breast cancer cases were diagnosed (25% of all cancers), and surprisingly 5.2 million cases of mortality were recorded, thereby making it the leading cause of death among women. In India, the incidence of breast cancer is rising. It is estimated that in 2008 there were 115,251 new cases of breast cancer with an age standardised incidence rate (ASR) of 22.9 per 100,000. Furthermore, by the year 2030 the number of new cases of breast cancer in India is estimated to reach approximately 200,000 per year [5].

Interestingly, it is the most recurring cancer among both more as well as less developed regions. Though, slightly higher number of cases has been observed in less developed regions (883,000 cases) than in more developed (794,000) regions among women (Figure 1) [10]. Variation of rate of incidences is almost four-fold across the world regions, the difference in the rates ranges from 27 per 100,000 in Eastern Asia and Middle Africa and 96 per 100,000 in Western Europe. The mortality rate is low in world regions because of the more favorable survival rate of breast cancer has been noted in developed regions [10], with rates ranging from 6 per 100,000 in Eastern Asia to 20 per 100,000 in Western Africa (Figure 1).

PROSTATE CANCER

It is the second most common cancer among men, 1.1 million men were diagnosed with prostate cancer in 2012 globally, out of which, almost 70% of the cases (759,000) occurred in more developed regions. Out of 1.1 million, there was an estimated mortality of around 307,000 [10].

Prostate cancer incidence rates are huge in Northern America and Australia/New Zealand [Age Standardized Rate (ASR) 111.6 and 97.2 per 100,000, respectively], and in Northern and Western Europe. In India also, the incidence of prostate cancer is on rise [16]. One of the major reasons is using Prostate Specific Antigen (PSA) testing and frequent biopsy of prostate cancer widespread in those regions. Incidence rates are also relatively high in some less developed regions, such as the Southern Africa (61.8), South America (60.1) and Caribbean (79.8) but on the contrary, low incidence rates have been observed in Asian populations with estimated rates of 10.5 in Eastern Asia and 4.5 in South-Central Asia [10]. Prostate cancer has been perceived to be mainly high in black populations (sub-Saharan Africa, ASRs 19-24 per 100,000 and Caribbean shows 29 per 100,000), and to be very few in number in Asia (2.9 per 100,000 in South-Central Asia) (Figure 2) [10].

GALLBLADDER CANCER

According to a recent report, 178,101 cases of incidence of gall bladder cancer (GBC) were diagnosed, out of which 142,813 died [10]. Incidences of GBC are low in number as compared to other malignancies. Eastern and Central Europe shows significant incidence of gall bladder cancer. Though, marked reduction has been observed over the years. Countries like Hungary, Germany, Sweden, UK, The Netherlands and France showed decreasing trend of mortality rates. Significant increase in mortality rates among men was seen only in Iceland [13].

GBC is very infrequent among people of North America. Hispanics and Native American Indians show the highest incidence rates among US population [18]. It was disclosed that an incidence of 1-2 cases per 100,000 populations are observed in the United States per year [14]. South American countries have the highest incidences of GBC throughout the world. Columbia, Chile, Costa Rica, Bolivia and Ecuador are known for high incidences. Out of these Costa Rica, showed a significant increase in mortality rate [13].

Australia is one of the countries having a declining trend for GBC. Indigenous population of South Australia has almost four fold chance of incidence than non-indigenous population. The basis of this finding has been attributed to genetic and environmental factors, but the true cause is still unknown [27].

GBC is one of the most prominent hepatobiliary malignant disease in east of Asia. India, Pakistan, Israel and Japan have high incidence rates (Figure 3) [14]. Northern and Eastern India shows higher prevalence [19]. A significant decline in men mortality rates has been seen in Japan and Hong Kong whereas Israel showed a decreasing trend in women mortality rates. Korea has shown a significant upward trend for GBC for both the sexes [13]. GBC is very rare in African populations and the incidence rate has been very low.

SIGNS AND SYMPTOMS

Signs and symptoms of breast cancer: Swelling of a breast, skin irritation or dimpling of breast or nipple pain, nipple retraction (turning inward), redness, scales, thickening of the nipple or breast skin and nipple discharge other than breast milk. Breast cancer can also spread to lymph nodes under the arm or around the collarbone and cause a lump or swelling there [2].

Signs and symptoms of prostate cancer: In the early stage of prostate cancer, usually no proper symptoms can be seen but sometimes prostate cancer does produce symptoms, often similar to those of diseases such as benign prostatic hyperplasia. This includes symptoms like increased urination at night, difficulty in starting and maintaining a steady stream of urine, blood in the urine and often accompanied with painful urination [22].

Signs and symptoms of gall bladder cancer: GBC shows certain signs and symptoms which is very useful in early detection. These include gallstones, pain in the upper right part of the abdomen, weight loss, raised bilirubin levels, jaundice, leukocytosis, pallor, ascites, gall bladder polyps, nausea and vomiting, fever, bowel obstruction and anomalous pancreaticobiliary junction [15].

RISK FACTORS

Risk factor determination is very important for understanding the pathogenetic mechanism resulting in geographic and ethnic variance and also defining strategies for treatment as well as prevention [14].

Breast Cancer Risk Factors

Heredity

BRCA1 and BRCA2: Mutations in the BRCA1 and BRCA2 genes are generally the cause of breast cancer. People suffering from mutations in the BRCA1 or BRCA2 genes have almost 80% risk of developing breast cancer. Breast cancers directly linked with BRCA1 or BRCA2 gene mutations mostly occur in younger women and affect both breasts [4].

Hormones

Natural Estrogen Exposure: Specific hormones associated with menstruation, such as estrogen and progesterone, also play an important role in certain breast cancers. Women with early age of menarche almost around 13 years old and younger and women with late onset of menopause around 55 years old and older may have an increased risk of breast cancer [4].

Hormone Replacement Therapy (HRT): Women undergoing estrogen and progesterone combined HRT therapy for almost five years, suffer from a much higher risk of developing breast cancer.

Oral contraceptive use: Women who use oral contraceptives may have a slightly higher breast cancer risk than those women who have never used oral contraceptives.

Race/Ethnicity: Specific genetic mutations are associated with increased breast cancer risk. Such mutations are found more frequently in populations with Ashkenazi Jewish ancestry compared to the general population. Overall, it has been found that white women are more likely to develop breast cancer whereas the African-American women are more likely to develop breast cancer at a younger age and to die of breast cancer than are white women [4].

Smoking: Cigarette smoking is known to increase the risk of breast cancer among women.

Physical Activity: Regular exercise reduces the breast cancer risk. Obesity may increase the risk of breast cancer, mainly after menopause, possibly due to the estrogenic impact of excess body fat.

Alcohol: Alcohol use has been revealed to be associated with increased risk of breast cancer.

Age: The breast cancer risk increase with increase in the age of women, about 2 out of 3 invasive breast cancers are found in women age 55 or older.

Breastfeeding: Some studies have found that women who do not breastfeed have higher risk of breast cancer.

Night work: Studies has suggested an association between women who work at night shifts and increased breast cancer risk [4].

Prostate Cancer Risk Factors

Age: The risk of prostate cancer is directly proportional with the age. Mainly 80% of prostate cancers are diagnosed in men who are 65 or older.

Race /ethnicity: Black men have a more risk of prostate cancer than white men. They develop prostate cancer at an earlier age and have been found to possess aggressive tumors that develop quickly. Hispanic men have a less risk of developing prostate cancer and dying from the disease than white men. Prostate cancer occurs mostly in North America and Northern Europe.

Heredity: Prostate cancer mostly begins when one or more genes in a cell undergo mutation. Prostate cancer that runs in a family, called *familial prostate cancer*, is less common (about 20%) and occurs because of a combination of shared genes and shared environmental or lifestyle factors [21].

Gall Bladder Cancer Risk Factors

Age: Incidence starts increasing after the age of 45 years and peaks at above 65 years. Male to Female ratio has been shown to be 1:3.8 [15].

Socio-economic background: Population belonging to lower socio economic background is found to be at a higher risk.

Dietary habits: Diet has certain effect on biliary tract cancers [7]. Population consuming oily foods and animal proteins and fats show higher risk than those ingesting vegetables and fruits. Also, higher the calorie intake, higher is the risk. Carbohydrate, protein and cholesterol show weaker association with GBC [20]. Proportion of GBC is higher among people having non-vegetarian diet. Diet containing channa and bhindi showed significant reduction in GBC incidence. Consumption of materials like urad dal, moong dal, milk, cottage cheese, butter, curd, mustard leaves, tamarind, pineapple and pomegranate resulted in higher incidences of GBC.

Tobacco: GBC is significant among tobacco users and smokers both in case of males as well as females.

Alcohol: Habit of consuming alcohol is suggestively associated with GBC risk. All types of alcohols except beer show elevated results.

Weight: Significant association is found between GBC and body weight.

Typhoid carrier status: Typhoid carrier status and GBC are significantly associated.

Gallstones: Around 70-80% of GBC cases carried gallstones.

Reproductive history: Among females GBC had an association with age of menarche, age of first & last child birth and pre-menstrual & post-menstrual status.

Drugs: Ceftriaxone, Octreotide and Thiazide diuretics also pose some effect [26].

Genetic Factors: GBC patients suffering from anomalous junction of the Anomalous Pancreaticobiliary Duct Junction show *K-ras* mutation [17]. Point mutations at exon 5 to 8 and deletions at locus 17p13 of *TP53* are responsible for GBC. Microsatellite instability, modifications in *TGFβRII* gene and under expression of retinoblastoma (Rb) and p16 are also some of the factors that contribute to gall bladder carcinoma. Promoter hyper methylation also affects *K-ras*, one of such promoters is *RASSF1A*, which in turn gets inactivated and leads to GBC. Chromosomal arms both long arm (5q, 6q, 9q, 13q and 16q) and short arm (1p, 3p, 5p and 17p) show loss of heterozygosity (LOH) in case of GBC [25].

Other risk factors: Apart from gallstones, ethnicity and female gender, associated with gallbladder cancer development are progressing age, gallbladder polyps, congenital biliary irregularities, neoplastic initiators, such as unknown endobiotic and exobiotic mutagens, or neoplastic promoters, such as chronic inflammation and infection. A relation has been found between *Salmonella typhi* and chronic bacterial infection of the gallbladder [17].

DIAGNOSIS

Physical Exam

In case of breast cancer, thorough examination is done to take in to account the presence of lumps, change in nipples or skin of the breast, enlarged lymph nodes and any change in texture or size [2, 3].

Mammography

It involves taking an x-ray of the breast in case of breast cancer. It gives a view of the concerned area and helps in confirming the results [2, 3].

In case of Prostate Cancer, a digital rectal exam can be done for diagnosis [22, 23].

PSA Testing

Prostate-specific antigen (PSA) test: PSA is a protein produced by cells of the prostate gland. The PSA test measures the level of PSA in a man's blood. For the testing of PSA level, a blood sample is sent to a laboratory for analysis and expressed in nanograms of PSA per milliliter (ng/mL) of blood. The blood level of PSA is often elevated in men with prostate cancer [23].

Imaging techniques

Various imaging tests involving the use of x-rays, magnetic fields, or sound waves have been determined for detecting several malignancies [9].

Ultrasound

In case of Breast cancer, ultrasound is generally focused on a specific area involved. It can be used to differentiate between solid mass and fluid-filled cysts [2, 3].

Prostate cancer involves the use of transrectal ultrasound for prostate biopsy as it gives a view of the tissues or structures that reflect relatively less of the ultrasound waves directed at them.

Ultrasound is one of the first imaging tests carried out on people showing the symptoms causing gall bladder cancer [9]. Polypoidal mass is exposed with this technique [14]. Presence of gallstones can also be detected. With the advent of Endoscopic or laparoscopic ultrasound, tumor detection and the extent of damage can be defined.

Magnetic resonance imaging (MRI) scans

Mammograms can be used together with MRI scans, in case of breast cancer, for the purpose of diagnosis [2, 3].

While in case of prostate cancer, MRI gives a very clear picture of the prostate thereby giving an idea as to how to proceed for the treatment [22].

Whereas in case of gallbladder cancer, various specific images of soft tissues of gall bladder can be provided by radio waves used in MRI scans [9]. Because MRI is less valuable in GBC detection, therefore, special type of MRI known as Magnetic Resonance Cholangio-Pancreatography (MCRP) is used to look at bile ducts and Magnetic Resonance Angiography (MRA) to look at blood vessels [14].

Computed tomography (CT) scan

A CT scan can be done to determine whether lymph nodes close by have been affected by prostate cancer [22, 23].

The CT scan uses an x-ray test to provide detailed cross-sectional images in case of gall bladder cancer [9]. This technique is used for showing tumors present in a particular area, determining the stage of the cancer, involvement of lymph nodes, liver and distant organs and also, to carry out guided needle biopsy [14].

Positron Emission Tomography (PET)

Fluorodeoxyglucose positron emission tomography (FDG-PET) scanning involves detecting tumor cells in gall bladder cancer who have taken up fluorodeoxyglucose [14].

TREATMENT

Surgery

Potentially curative surgery is carried out when there is a good chance that the cancer can be removed by surgery.

Breast cancer surgery is of three types. First is *mastectomy*, which involves removal of a part area affected. Second is *lumpectomy*, which is concerned with only the removal of lumps and third is *quadrantectomy*, removal of a quarter of the breast [2]. Main type of prostate cancer surgery is *radical prostatectomy*, which involves removing the whole of prostate and some tissues along with it [22].

Laprosopic cholecystectomy is a very popular method of potentially curative surgery for complete removal of gall bladder. In this technique, a small incision is made so that a laproscope, with an attached video camera, can be inserted in one's body. This enables the surgery to be carried out smoothly [9].

Radiation Therapy

This therapy involves high energy radiations for killing of cells. There are two categories of radiation therapy, namely, external and internal radiation therapy. External involves radiation being directed towards the cancer from outside of the body and in internal therapy, radioactive materials are introduced inside or near the cancer using needles, catheters, wires etc. [8].

Therapies involved in breast cancer are accelerated breast irradiation, 3-dimensional conformal radiotherapy (3D-CRT), interstitial brachytherapy and intracavitary brachytherapy [2].

Prostate cancer radiation therapy involves techniques like 3-dimensional conformal radiation therapy (3D-CRT), intensity modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT), proton beam radiation therapy, permanent brachytherapy and temporary brachytherapy [22].

Newer techniques have come into play for treating GBC, such as, 3-dimensional conformal radiation therapy (3D-CRT), intensity modulated radiation therapy (IMRT) and proton beam radiation therapy [9].

Chemotherapy

This is a treatment with anti-cancer drugs to put a restriction on the growth of cancerous lesions. Most commonly used drugs for breast cancer are CAF/FAC (cyclophosphamide, doxorubicin and 5-FU), TAC (docetaxel, doxorubicin, and cyclophosphamide), AC → T (doxorubicin and cyclophosphamide followed by paclitaxel or docetaxel), FEC → T (5-FU, epirubicin, and cyclophosphamide followed by docetaxel or

paclitaxel), TC (docetaxel and cyclophosphamide) and TCH (docetaxel, carboplatin, and trastuzumab for HER2/neu positive tumors) [2]. Some of the chemotherapeutic Drugs used for treating prostate cancer are Docetaxel, Cabazitaxel, Mitoxantrone, Estramustine, Doxorubicin, Etoposide, Vinblastine, Paclitaxel, Carboplatin and Vinorelbine [22].

A number of drugs have been designed for GBC. Gemcitabine, Capecitabine, 5-fluorouracil (5-FU), Cisplatin and Oxaliplatin are often used for treating GBC [9]. These can be given intravenously (*i.v.*), intramuscularly (*i.m.*) or by ingesting them through the mouth [8]. Several new drugs have been created who target tumor blood vessels, such as Bevacizumab. Some drugs that target EGFR, such as cetuximab and Iapatinib are beneficial against GBC [22].

Hormonal Therapy

Hormonal therapy for breast cancer can be achieved through drugs that block estrogen (Tamoxifen, Toremifen and Fulvestrant) and treatments to lower estrogen levels (Aromatase inhibitors and ovarian ablation) [2].

Therapy given for prostate cancer includes treatment to lower androgen levels (Orchiectomy, Luteinizing hormone-releasing hormone analogs, Luteinizing hormone-releasing hormone antagonists), drugs inhibiting normal functioning of androgens (Anti-androgens) and androgen suppressing drugs [22].

CONCLUSION

In 2008, Breast cancer was the second leading cancer among women globally but within a span of 5 years, it has become the leading cause of death among women. Similarly, Prostate cancer has been the second leading cause of death among men after the lung cancer. This shows that these two cancers are highly responsible for the peak in cancer mortality globally. On the other hand, Gall Bladder cancer is very rare but shows a very high mortality rate. Also, it is one of the few carcinomas which are higher in women. This shows that though it is rare in nature but takes a heavy toll on human population. It is necessary to give importance to this cancer so that it may not suffer the same fate as breast cancer. Early detection is the key to curb this problem. Screening can be done to detect these cancers as early as possible. It is an essential step to lower the incidence as well as mortality rates. Mammography and clinical breast exam can be conducted for females (starting at the age of 40) every year for breast cancer detection whereas Prostate cancer can be easily detected by performing PSA testing of a man's blood sample. Besides this, another option for proper screening of prostate cancer is a digital rectal exam. In the case of carcinoma of Gall Bladder, certain liver and blood test are available. The concentration of substances like bilirubin, alkaline phosphatase, albumin etc. can be determined. Although, these tests are available but even then it is found at a very advanced stage, i.e., when gall bladder needs to be removed or certain symptoms are seen. Thus, incidence and mortality of these cancers can be curtailed by making people aware of how these cancers can be prevented by early detection and the associated risk factors along with imparting personalized therapy to the patients.

ACKNOWLEDGEMENTS

Authors are grateful to Dr. Ashok K. Chauhan, Founder President, and Mr. Atul Chauhan, Chancellor, Amity University Uttar Pradesh for their valuable guidance and kind support.

REFERENCES

- [1] Bray F., Ren J. S., Masuyer E., Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008, *Int. J. Cancer*, 2013, 132 (5): 1133–1145.
- [2] Available online at: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003090-pdf.pdf>
- [3] Available online at: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003165-pdf>
- [4] Available online at: http://athenacarenetwork.org/wp-content/uploads/2012/08/Quick_Links-Risk-Assessment-Talking-Points.pdf
- [5] Datta K., Choudhuri M., Guha S., Biswas J. Breast Cancer Scenario in a Regional Cancer Centre in Eastern India over Eight Years - Still a Major Public Health Problem, *Asian Pacific Journal of Cancer Prevention*, 2012, 13: 809-813.
- [6] Ferlay J., Shin H. R., Bray F., GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide, (IARC). 2012. Available from: <http://globocan.iarc.fr>.
- [7] Fraumeni J.F. Jr. Cancers of the pancreas and biliary tract: epidemiological considerations, *Cancer Research* 1975, 35: 3437-3446.
- [8] Available online at: <http://www.cancer.gov/cancertopics/pdq/treatment/gallbladder/Patient/page1/AllPages/Print>
- [9] Available online at: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003101-pdf.pdf>
- [10] Available online at: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
- [11] Available online at: http://globocan.iarc.fr/Pages/fact_sheets_population.aspx
- [12] Hamdani N. S., Qadri S. K., Aggarwalla R., Bhartia V. K., Chaudhuri S., Debakshi S., Baig S. J., Pal N. K. Clinicopathological Study of Gall Bladder Carcinoma with Special Reference to Gallstones: Our 8-year Experience from Eastern India, *Asian Pacific J Cancer Prev* 2013, 13 (11): 5613-5617.
- [13] Hariharan D., Saied S., Kocher H. M. Analysis of mortality rates for gallbladder cancer across the world, *International Hepato-Pancreato-Biliary Association* 2008, 10: 327-331.
- [14] Hundal R. and Shaffer E. A. Gallbladder cancer: epidemiology and outcome, *Clinical Epidemiology* 2014, 6: 99-109.
- [15] Khan I., Panda N., Banerjee M., Das R. Epidemiological Factors in Gall Bladder Cancer in Eastern India-A Single Centre Study. *Indian J Surg Oncol* 2013, 4(1): 67–72.
- [16] Lalitha K., Suman G., Pruthivish S., Mathew A., Murthy N. S. Estimation of Time Trends of Incidence of Prostate Cancer – an Indian Scenario, *Asian Pacific J Cancer Prev*, 2012, 13 (12): 6245-6250.
- [17] Lazcano-Ponce E. C., Miquel J. F., Herrero R., Ferrecio C., Wistuba I. I., Alonso de Ruiz P., Urista G. A., Nervi F. Epidemiology and Molecular Pathology of Gallbladder Cancer, *CA Cancer J Clin*. 2001, 51(6): 349-364.

- [18] Michaud D. S. The epidemiology of pancreatic, gallbladder, and other biliary tract cancers, *Gastrointestinal Endoscopy* 2002, 56 (6): S195-S200.
- [19] Murthy N. S., Rajaram D., Gautham M.S., Shivraj N. S., Pruthvish S., George P. S., Mathew A. Trends in incidence of gallbladder cancer – Indian scenario, *Gastrointestinal Cancer: Targets and Therapy* 2011, 1: 1-9.
- [20] Pandey M., Shukla M., Shukla V. Diet and Gallbladder Cancer, *Indian Journal of Medical & Paediatric Oncology* 2008, 29 (1): 6-7.
- [21] Available online at: <http://www.cancer.net/cancer-types/prostate-cancer/risk-factors-and-prevention>
- [22] Available online at: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003134-pdf.pdf>
- [23] Available online at: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003182-pdf.pdf>
- [24] Siegel R., Naishadham D., Jemal A. *Cancer Statistics 2013*, *CA Cancer J Clin.* 2013, 63: 11-30.
- [25] Singh S., Ansari M. A., Narayan G. Pathobiology of Gallbladder Cancer, *Journal of Scientific Research* 2012, 56: 35-45.
- [26] Stinton L. M. and Shaffer E. A. Epidemiology of Gallbladder Disease: Cholelithiasis and Cancer, *Gut and Liver* 2012, 6(2): 172-187.
- [27] Tipnis R., Curnow S., Creamer G., Jacob J. Incidence of Gall Bladder Cancer on Central Australian Populations, *Austral-Asian Journal of Cancer* 2011, 10 (2): 79-80.

Figure 1: Breast Cancer Estimated Incidence, Mortality and 5-year Prevalence Globally (per 100,000 women) in 2012. Source: [10]

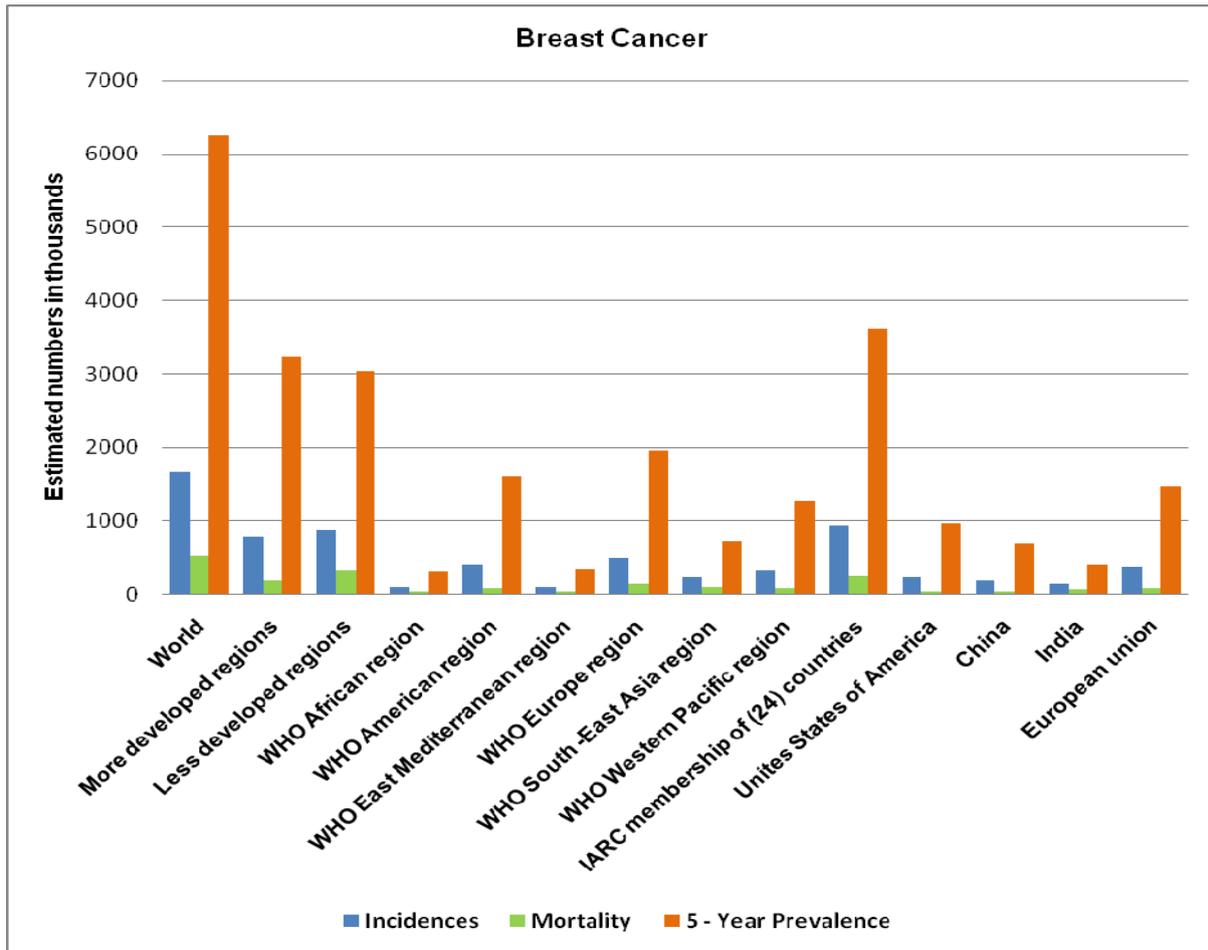


Figure 2: Prostate Cancer Estimated Incidence, Mortality and 5-year Prevalence Globally (per 100,000 men) in 2012. Source: [10]

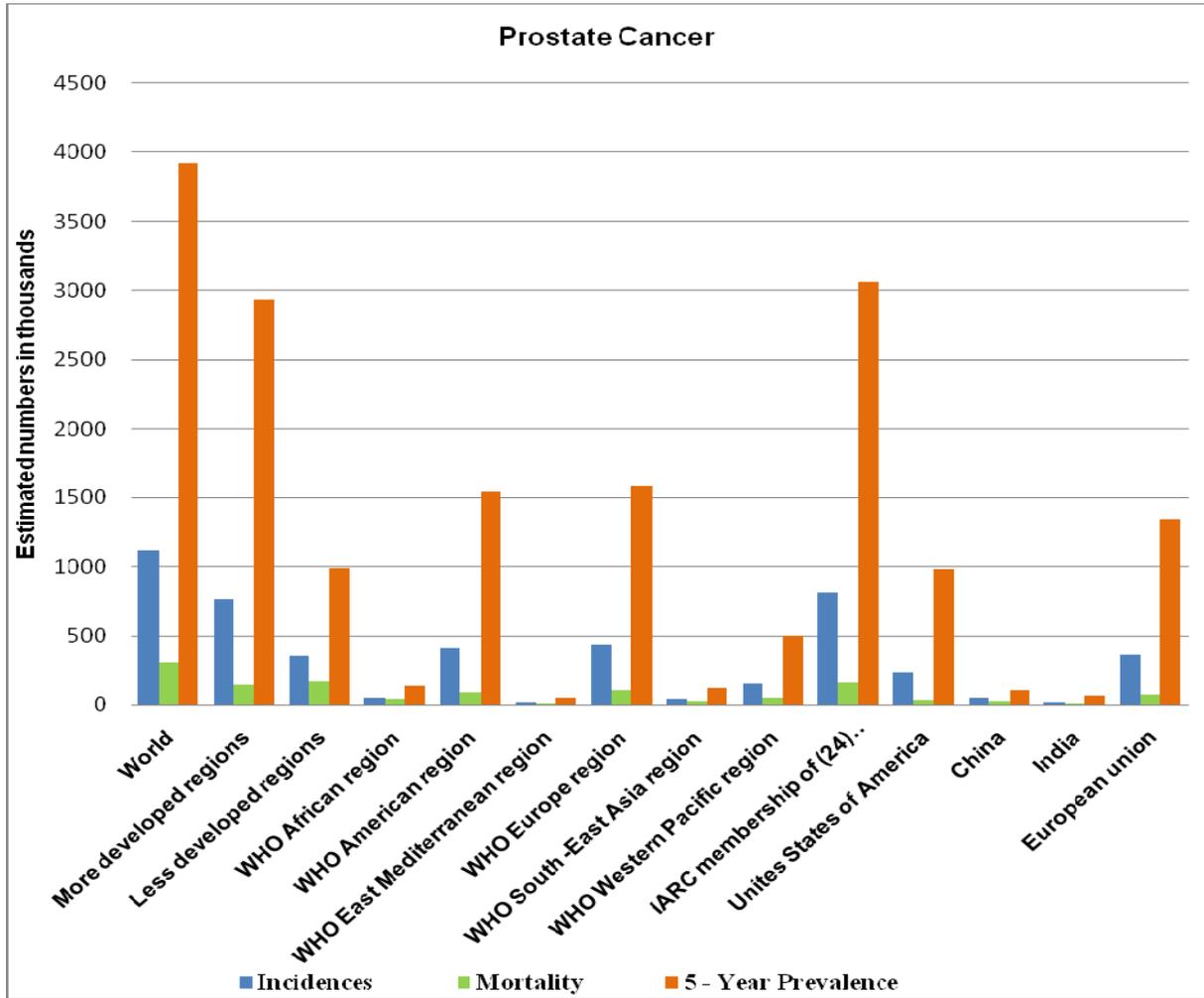


Figure 3: Incidence of Gall Bladder Cancer Globally (per 100,000). Source: [14]

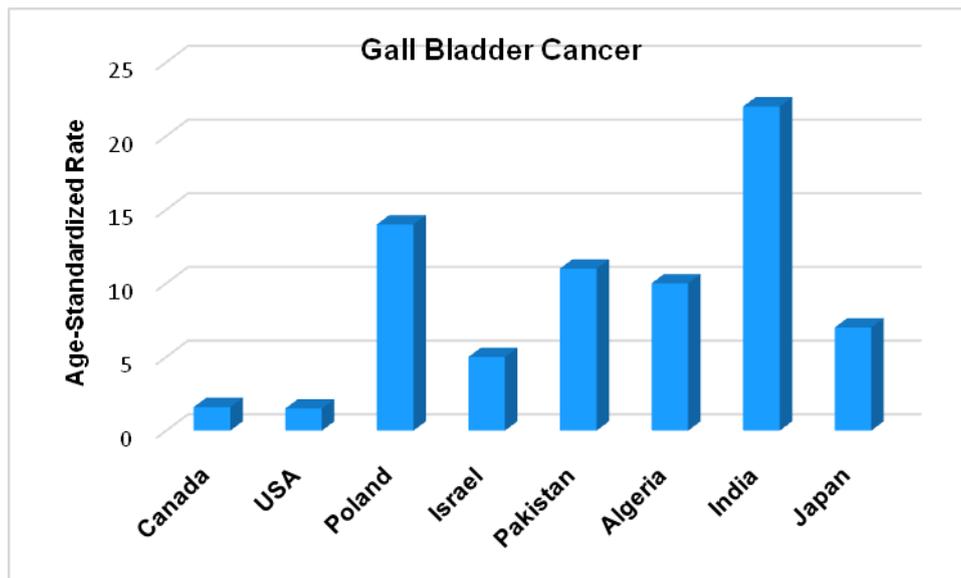


Table 1: Estimated Incidence, Mortality and 5-year prevalence of Breast, Prostate and Gall Bladder Cancer per 100,000 population of India in 2012. Source: [10, 11]

Cancer	Incidence	Mortality	5-Year Prevalence
Breast	144,937	70,218	396,991
Prostate	19,095	12,231	63,818
Gall Bladder	18,787	15,866	22,892