

Demography and disease characteristics of prostate cancer in India

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ABSTRACT

Introduction: The incidence of prostate cancer has shown significant variation across the globe. Though the prevalence and characteristics of this disease have been extensively studied in many countries, data regarding the true incidence of prostate cancer in India is limited.

Materials and Methods: MEDLINE publications from 1990 to 2014 were searched and reviewed and compiled to assess the demographic profile of prostate cancer in India and characteristics unique to this disease in India.

Results: The limited data available on prostate cancer showed significant differences in incidence, precipitating factors, and disease characteristics of prostate cancer in India.

Conclusions: Since India would be having more number of cases of prostate cancer than most others in the years to come, adequate population-based data regarding the demography and disease characteristics of this disease are of paramount importance in this country.

Key words: Demography, India, prostate cancer

INTRODUCTION

Prostate cancer is primarily a disease of the elderly with more than three quarter of the cases occurring in men above 65 years of age. This disease has become a major health problem globally during the last few decades. Studies have shown that prostate cancer is the second most frequently diagnosed cancer in men worldwide and the fifth most common cancer overall.^[1] It is disheartening to note that approximately 4.04 million years of healthy life are lost globally due to prostate cancer alone. It is also the sixth leading cause of cancer deaths in men.^[2] Worldwide, prostate cancer is projected to have the largest proportionate increase in cancer cases in men by 2020.

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The incidence of prostate cancer has shown significant variation across the globe. The highest rates of prostate cancer are reported in Australia/New Zealand (104.2/100,000), Western and Northern Europe, and North America presumably due to prostate-specific antigen (PSA) screening being done widely in these regions.^[3] However, the mortality rates of prostate cancer tend to differ in various countries. The mortality has been reported to be the highest in low- to middle-income communities of parts of South America, the Caribbean, and sub-Saharan Africa.^[4] In the Asian countries, prostate cancer incidence has been reported to vary from 3.0/100,000 in Iran to the highest of 20.3/100,000 in the Philippines in the year 2000.^[5] There has been a consistent increase in the age-standardized incidence rates (ASIRs) of prostate cancer in Asian countries over the last few decades, particularly in Singapore, China, Malaysia, and Japan. This has been reported to be due to changes in diet and other lifestyle factors in these countries.^[6,7] Zhang *et al.*^[8] also reported that the average mortality-to-incidence rate

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ratio (MR/IR) of prostate cancer was 0.57 in China compared to 0.13 in North America, indicating that in China, at the time of diagnosis, most cancers were in the advanced stage and therefore, these patients had a short survival time thereafter. However, it is interesting to note that in another Asian country, namely, the Republic of Korea, the ASIR of prostate cancer was reported to be small.^[9]

In India, data regarding the true incidence of prostate cancer is limited mainly due to the fact that this entity is not a notifiable disease and there are only a handful of population-based cancer registries in India. The number of community-based studies on prostate cancer is also limited in this country.

MATERIALS AND METHODS

We searched the MEDLINE database for publications from 1990 to 2014 and compiled the demographic profile of prostate cancer in India. Out of the 126 publications reviewed, 56 references have been cited in this paper while the rest of the papers did not have relevant data.

CENSUS OF INDIA 2011 - THE HIGHLIGHTS

The Census of India released on July 15, 2011^[10] revealed various interesting statistics relevant to the pattern of prevalence and other disease characteristics of prostate cancer. India has a population of 121.0 crores, out of which 68.84% reside in rural areas and 31.16% in urban areas. More than 50% of the population is below the age of 25 years and more than 65% is below the age of 35 years. It is expected that in 2020, the average age of an Indian will be 29 years compared to 37 years for a Chinese and 48 years for a Japanese. 9.8 crore males are over 50 years of age and the average life expectancy has increased to 70 years. All these demographic data will have a bearing on the changing incidence and pattern of prostate cancer in the ensuing decade.

PROSTATE CANCER DEMOGRAPHY IN INDIA

There is an increasing trend in the burden of noncommunicable diseases like cardiovascular disease, diabetes mellitus, and cancers as evidenced by the various demographic and epidemiological studies conducted in India. Oral and esophageal cancers have the highest incidence, whereas rectal, prostate, and lung cancers have the lowest.^[11] It has been reported that although the cancer rates in India are lower than those seen in Western countries, increase in life expectancy and changes in lifestyles increase the rates of cancers in this country, particularly prostate cancer. Lathika *et al.*^[3] analyzed the time trends in the incidence of prostate cancer for different age groups of the Indian population reported in Indian cancer registries, using relative difference and regression approaches covering the following

areas: Ahmedabad, Bangalore, Chennai, Delhi, Mumbai, Karunagappalli, Nagpur, Pune, and Thiruvananthapuram. The estimated age-adjusted incidence rates (AARs) of prostate cancer in India as a whole was 3.7/10⁵ persons during the year 2008. However, the regional variation of AAR was remarkable. It was found to be 0.8 in the state of Manipur (excluding Imphal) while in Delhi, the rate was 10.9/10⁵ person-years. The mean annual percentage change (MAPC) in the crude incidence rates ranged from 0.14 in Ahmedabad to 8.6 in Chennai. Peak incidence was observed in the age group above 65 years, indicating that prostate cancer was a cancer of the elderly. Chennai also recorded the highest MAPC of 5.66 in the age group of patients above 65 years. The estimated annual percentage change (EAPC) in the AAR ranged 0.8-5.8 in the various registries. Increase in the trend was seen in men aged 55-64 years in Bangalore, Chennai, and Mumbai during 1983-2002 and in the 35-44 years age group in metropolitan cities such as Delhi and Mumbai. This revealed an increasing trend in the incidence of prostate cancer and the annual percentage change ranged 0.14-8.6. However, one of the limitations of these cancer registry-based studies was that these registries were mostly urban-based and the data available from the rural population were very little. Projected cases of prostate cancer all over India for the periods 2010, 2015, and 2020 were estimated as 26,120, 28,079, and 30,185, respectively.^[12] Jain *et al.* also reported a wide variation in annual percentage change of prostate cancer in various population-based cancer registries of India, ranging from 3.4% in Bangalore to 11.6% in Kamrup District in Assam.^[13] Apart from the variations in reporting and documentation of cases, no clear-cut reasons for this vast variation in MAPC across the various regions in India have been identified in any of these studies.

Yeole^[14] had analyzed and reported the trends in prostate cancer in five population-based cancer registries (Mumbai, Chennai, Bangalore, Delhi, and Bhopal) over a period of two decades. It was found that the AAR for prostate cancer in Mumbai registry was 6.3/100,000 in 1988, with the corresponding figures in Delhi, Bangalore, Chennai, and Bhopal being 5.8, 5.1, 2.5, and 2.2, respectively. In 2003, there was a significant increase in the AAR in these registries to the tune of 7.2, 8.2, 6.8, 3.9, and 5.9 per 100,000 people, respectively. The rank of prevalence of prostate cancer when compared to other cancers also significantly increased in the registries during these two decades; for e.g., prostate cancer ranked eighth in its prevalence in Mumbai in 1988, whereas it ranked fourth in 2003 in the same registry. The maximum increase in AAR over the entire period of observation was noted for Chennai registry (4.95%) and the least for Mumbai registry (0.89%).

There have been variations in the reported incidences of prostate cancer in the eastern parts of India. Sen *et al.*^[15] had reported a very low incidence (4.2% of all malignancies) of

prostate cancer in Kolkata during the period of 1998-1999 from a population-based cancer registry. However, Chatterjee^[16] analyzed prostate cancer profile in the population of West Bengal from 2003 to 2010 and showed that the frequency of this cancer was increasing with the overall 5.71% incidence and this rise was moderate during 2003-2006 but it rose drastically from 2007 (17.76%) and reached the maximum peak (28.97%) in 2010. She also found a higher prevalence of prostate cancer in persons with blood group A followed by blood group B and blood group O. The exact reason for this significant drastic increase in the incidence of prostate cancer in this region was again unknown. It could be presumed to be due to the increase in awareness on the part of the treating doctors and the public, leading to better identification of this disease. The author also attributed the increase in the number of new prostate cancer cases to the growth in the size of the population, especially in the proportion of elderly persons. It was also observed that prostate cancer rate was increasing with 5.71% incidence in Eastern India as a whole.

Tyagi *et al.*^[17] have reported their observation on the incidence and risk factors of prostate cancer on patients registered by the Delhi population-based cancer registry during the period from January 1998 to December 2000. The mean age of patients with prostate cancer was 69.7 years. They reported that over the years, prostate cancer had become the fifth most common cancer in Delhi. These authors also observed that the incidence of prostate cancer was higher among North Indians compared to South Indians.

Swaminathan *et al.*^[18] in their study observed that the average annual age-standardized rate for prostate cancer had significantly increased by 47% during the period of 2002-2006 in Chennai compared to the previous years. They had observed that prostate cancer had become the ninth most common cancer in Tamil Nadu.

Herbert *et al.*^[19] compared data available from various cancer registries and observed that the average annual cancer incidence rate for prostate cancer in India ranged 5.0-9.1 per 100,000/year, whereas the comparative rate in the United States were 110.4 for whites and 180.9 for blacks. Of all prostate cancers, 85% were detected late (stages III and IV) in India in contrast to the United States where only 15% were diagnosed in the late stages. A notable difference was also observed between the rural and urban areas. The rural registry at Barshi in western Maharashtra registered the lowest ASIR of 1.5/100,000; while the registry in Mumbai had higher incidence rates of around 7.1/100,000. In 1994, Sharma *et al.*^[20] had also reported that the highest incidence of prostate cancer in the country (11.6/100,000) was in the urban city of Jaipur. These indicate that there exist significant differences in the incidence of prostate cancer in the rural and urban areas in India. This again could be either due to the lack of awareness about this disease in the

society or due to the poor reporting and documentation of cases in the rural populations.

RISK FACTORS FOR PROSTATE CANCER - THE INDIAN SCENARIO

India is a land of diversity. The religions, cultures, environment, literacy rates, and food habits of the society vary from one region to another. These variations can have a significant bearing on the incidence of prostate cancer in various regions across the country. There are several risk factors implicated in the causation of prostate cancer, namely, positive family history,^[21] history of diabetes mellitus,^[22] height, weight and obesity,^[23] smoking habit, physical activity,^[24] body mass index (BMI),^[25] and vasectomy.^[26] However, in India, the studies on the actual role of these risk factors in the causation of prostate cancer are limited.

Ganesh *et al.*^[27] reviewed prostate cancer cases registered in Mumbai and found that the average ages for the cases and controls were 64 years and 46 years, respectively. Literacy rate was similar in both the groups. An equal proportion of cases and controls (13.8%) had a family history of prostate cancer. History of diabetes mellitus was fourfold among the cases and history of hypertension was threefold among the cases as compared to the controls. Those with BMI <24.9 had twice the enhanced risk for prostate cancer when compared to those with BMI >25. The number of children and vasectomy did not contribute to any significant risk in this study. Consumers of betel leaf with or without tobacco and pan masala, gutka chewers, smokers, and alcoholics also did not show any significant increased risk. Similarly, consumption of raw vegetables, meat, fish, tea, coffee, etc., also did not result in any additional risk of prostate cancer. This is contrary to the studies conducted in 2010 by Huncharek *et al.*^[28] which showed an increased risk of prostate cancer for chronic smokers. Interestingly, another study conducted earlier by Terry *et al.*^[29] had indicated a reduced risk of prostate cancer for fish eaters. The association of family history of cancer and prostate cancer risk seen in a previous study^[21] was also not observed in these studies.

Tyagi *et al.*^[17] also observed that there was no statistically significant association between family history of cancer and prostate cancer. However, past smoking habit and current alcohol consumption, especially consumption of whisky, significantly increased the risk of prostate cancer. The risk of prostate cancer reduced with the increasing dietary consumption of tea, citrus fruits, melons, eggs, fish, and sunflower oil. Though an increased risk of prostate cancer was evident among vasectomized men, the association was not statistically significant. Production of carcinogenic heterocyclic amines during cooking of red meat and pyrolysates during cooking of meat over charcoal/smoke had been attributed as the reason for increased prostate carcinogenesis in the nonvegetarians.^[30] A₂ allele of the

CYP17 polymorphism has also been reported to be associated with an increased risk of prostate cancer in smokers and nonvegetarians.^[31]

Singh *et al.* in 2013^[32] studied the relationship of lifestyle, age, and BMI with PSA levels in benign prostatic hyperplasia (BPH) and prostate cancer in the North Indian population. They found that the mean age of prostate cancer patients (67.56 ± 5.72 years) was significantly higher than that of BPH patients (63.56 ± 7.92 years). The prevalence of hypertension, smoking, use of tobacco, and alcohol consumption was similar in both the groups. However, there was no significant effect of BMI on the risk of prostate cancer that is in contrast to the findings of Amling *et al.*^[33] and Freedland *et al.*^[34] who had earlier studied the positive correlation of obesity to prostate cancer.

A large part of the Indian population is involved in agriculture and associated industries. Therefore, these people are potentially exposed (occupationally or environmentally) to some types of pesticides, either directly or indirectly. In the majority of instances, there exist only poor safety measures during the application and handling of these carcinogenic compounds. This could lead to widespread dispersion of these harmful and carcinogenic compounds, causing toxicity to human beings.^[35] Studies conducted by Banerjee *et al.*^[36] reported that some of these pesticides, mainly organochlorine pesticides (OCPs), possessed estrogenic properties and could be called xenoestrogenic pesticides. OCPs such as 1,1,1-hexachlorocyclohexane (HCH), dieldrin, and endosulfan were found to be the most commonly used xenoestrogenic OCPs in India. He further reported that since prostate cancer was an estrogen-dependent cancer, these pesticides might increase the risk of prostate cancer incidence in the population exposed to these carcinogenic agents.

PROSTATE CANCER PECULIARITIES IN NONRESIDENT INDIAN COMMUNITIES

There have been a few interesting reported on the demography and peculiarities of prostate cancer in nonresident Indians staying in countries worldwide. Tewari *et al.*^[37] analyzed the pathological characteristics of prostate cancer in 2,367 men who underwent robotic-assisted radical prostatectomy in the United States between Jan 2005 and July 2010 by a single surgeon. It was found that a significantly greater percentage of Asian Indians compared to Caucasians had extraprostatic extension (32.3 vs 16.5 ; $P = 0.01$), indicating more advanced cancer in this group. However, the biochemical recurrence rates (BCRs) were not significantly different in the two groups at a median follow-up of 16 months (94.6% vs 95.4%). Patel *et al.*^[38] also found that South Asian men had a significantly higher rate of positive surgical margins and positive nodal status after radical prostatectomy, whereas the

Gleason score was not significantly different in the various groups he studied.

Some studies have shown striking variations in the pattern of incidence of prostate cancer in various races. In the United States, African American men were seen to be at the highest risk of developing prostate cancer, with an annual incidence of $178/100,000$ while Asian Americans had a lesser annual incidence of $88.3/100,000$.^[39,40] More interestingly within this subgroup, the South Asian population (Indians, Pakistanis, Nepalese, Bangladeshis, and Sri Lankans) representing the third largest Asian American population in the United States had the least incidence of prostate cancer ranging $3.9-9.1/100,000$.^[19,40,41] These authors implicated the differences in diet and availability of screening methods to be the reason for the lower incidence of prostate cancer in this population.

Jain *et al.*^[42] observed that compared to the rates in native Asian Indians, the rate of cancer in South Asians in California was higher for all sites except oropharyngeal, esophageal, and cervical cancers. This variation could be associated with screening and tobacco habits rather than true differences in the underlying risk. South Asian men in California experienced 15-fold increase in the risk of prostate cancer as compared to Indian males.

Metcalfe *et al.*^[43] studied the risk of prostate cancer among South Asian men (men of Indian, Bangladeshi, and Pakistani origins) in four areas of Southern England and found that the prostate cancer rates in these patients were significantly lower (nearly 20%) compared to the white community (age-adjusted rate ratio 0.81; 95% confidence interval 0.65-1.00); however, the mean age of presentation with prostate cancer was lower in South Asian men (69 ± 9.2 years vs 73 ± 8.8 years). It has been reported that this disparity could be due to poor access of patients to the health care system, resulting in nonreporting of the disease or genuinely due to the greater protection of South Asian men due to exposure to sunlight during early childhood^[44] and lowered serum vitamin D levels in South Asians residing in the United Kingdom.^[45]

PSA LEVELS IN PROSTATE CANCER IN INDIA

PSA has been widely used as a diagnostics tool in the screening for prostate cancer. Though PSA level is known to vary with age and various age-adjusted nomograms of PSA values are available, it is not clear whether these reference values for PSA could be applicable in the Asian population, particularly the Indian population. This is because the PSA levels can vary in various ethnic groups. A study by Sin-Eng Chin *et al.*^[46] showed that the median PSA level in the Chinese, Malay, and Indian ethnic groups in Singapore were not different. They further observed that the PSA values

positively correlated with age and the mean values were lower than the PSA levels noted in the white population in the United States. However, the predictive values of PSA in detecting prostate cancer was found to be quite similar to those in Western Countries in another study by Mochtar and Andika.^[47] Malati and Kumari^[48] suggested a reference value for PSA in healthy males aged 20-89 years belonging to a subpopulation of Andhra Pradesh in South India. The results revealed lowest concentration of 95 percentile serum PSA in Indian males compared to other populations globally.

Ganpule *et al.*^[49] in 2007 also published their observations on age-specific PSA and PSA density values in a community-based Indian population in Gujarat. They observed that the mean PSA values increased from 2.1 ng/mL in the age group of 40-49 years to 5.0 ng/mL in the age group of >70 years. Similarly, the mean PSA density also increased from 0.15 to 0.2 ng/mL in the same age group of patients. Though PSA has been regarded as a useful tool for the early detection of prostate cancer, Dubey^[50] seriously doubted the utility of this tool for screening prostate cancer in Indian males due to the low incidence of this particular disease in this country. They also suggested the need for local guidelines and recommendations for mass screening, especially in elderly males above the age of 50 years in India.

Shah *et al.* in 2011^[51] in a hospital-based study comparing four ethnic groups in India based on their origin, namely, Indo-Nepalese, Tibeto-Nepalese, indigenous, and others found that the free PSA (f PSA) levels correlated fairly well with the age of the patient, but not with the ethnicity. The mean f PSA levels (ng/mL) among the four age categories (<45 years, 45-60 years, 60-75 years, and >75 years) were 0.49 ± 0.13 ng/mL, 0.69 ± 0.10 ng/mL, 1.94 ± 0.04 ng/mL, and 2.33 ± 0.43 ng/mL, respectively.

Atish *et al.*^[52] evaluated the free-to-total PSA (f/t PSA) ratio to distinguish BPH and prostate cancer in the age group of 40-75 years in Chennai, Tamil Nadu. They found that f/t PSA ratio was decreased significantly in prostate cancer compared to BPH. One study has shown that a cutoff for biopsy in symptomatic men with negative digital rectal examination (DRE) in India could safely be raised to 5.5 ng/mL, which could avoid subjecting 10% of men to undergo unnecessary biopsy.^[53]

Thakur *et al.*^[54] have also suggested the utility of f/t PSA ratio in the diagnosis of prostate cancer PSA levels in the Indian population. Malati *et al.*^[55] in 2006 studied the serum total PSA levels in 583 healthy males, 1,090 patients with BPH, and 651 patients with adenocarcinoma prostate in Andhra Pradesh in South India. They found that the PSA level was significantly high in BPH patients and adenocarcinoma prostate patients when compared to healthy males. Other than the abovementioned limited community-based Indian population studies, there have been no authentic reports

on PSA nomograms, Gleason's scoring pattern, and the difference in biochemical recurrence among those who underwent definitive treatment in various ethnic and other population subsets in this country.

CONCLUSIONS

The actual incidence of prostate cancer in India and in nonresident Indians is lower than that in the Western populations. Within India, prostate cancer has a wide variation in incidence, disease characteristics, and mortality, with the incidence being more in the urban population. Incidence of the disease is increasing in various parts of India. Changes in the diagnostic modalities, increased awareness among the public, and changing lifestyles may be responsible for much of the observed change. The lack of good population-based data in the country limits the ability of researchers to understand and report on the actual pattern and distribution of this disease. Meticulous implementation of registration and reporting mechanisms may improve knowledge regarding prostate cancer in India.

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Conflicts of interest

There are no conflicts of interest.

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