MINI-REVIEW

Epidemiology of Prostate Cancer

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Abstract

Prostate cancer is the most common malignancy among males worldwide, and is the second leading cause of cancer death among men in United States. According to GLOBOCAN (2012), an estimated 1.1 million new cases and 307,000 deaths were reported in 2012. The reasons for the increase of this disease are not known, but increasing life expectancy and modified diagnostic techniques have been suggested as causes. The established risk factors for this disease are advancing age, race, positive family history of prostate cancer and western diet (use of fat items). Several other risk factors, such as obesity, physical activity, sexual activity, smoking and occupation have been also associated with prostate cancer risk, but their roles in prostate cancer etiology remain uncertain. This mini-review aims to provide risk factors, disease knowledge, prevalence and awareness about prostate cancer.

Keywords: Prostate cancer - risk factors - epidemiology

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Introduction

Prostate cancer is the fourth leading cancer in both sexes and the second most common cancer in males. It was estimated that about1.1 million men worldwide of prostate cancer will be diagnosed in 2012, which is 15% of the malignances diagnosed in men and the estimated number of deaths will be almost 307,000 (Ferlay et al., 2015). Prostate cancer is the second most common cancer among Americans. It is estimated that about 220,800 new cases of prostate cancer will be diagnosed in the United States in 2015 that is 26% of all the malignances among males and the estimated number of deaths will be almost 27,540. A man's life time risk of developing prostate cancer is one out of seven (Siegel et al., 2015). The global burden of prostate cancer is expected to raise 1.7 million new cases and 499,000 deaths by 2030 due to growth and aging of the worldwide population (Ferlay et al., 2010).

Risk Factors

Age and ethnicity

Prostate cancer is a disease of elderly men. Almost 6 cases in 10 are diagnosed at the age of 65 years or later. It is rare before the age of 40, but the chance of developing prostate cancer rises rapidly after the age of 50. The average age at the time of diagnosed is almost 66 years (American Cancer Society, 2015). From 2007-2011, approximately 0.6% of prostate cancer cases were diagnosed between 35 and 44; 9.7% between 45 and 54; 32.7% between 55 and 64; 36.3% between 65 and 74; 16.8% between75 and 84; and 3.8% for 85 years of age or more (Howlader et al., 2014). The age especially 55 years and above had almost 17-fold higher risk of developing prostate cancer as compared to age less than 55 years (Bashir et al., 2014). Age was positively associated with prostate cancer risk, having odds ratios and 95% CI 5.35 and 2.17-13.19, respectively (Pourmand et al., 2007).

African-Americans have the highest rates of prostate cancer in the world (223.0 per 100,000 men). The incidence among African-Americans is about 60% higher than whites (139.9 per 100,000 men). The incidence rate for all races is 147.8 per 100,000 men. Moreover for the period 2007 to 2011, the mortality rate for African-Americans was 2.4 times higher than whites (Howlader et al., 2014). Table 1 shows the SEER incidence and U.S. mortality age adjusted rates by race/ethnicity from 2007 to 2011. Wide variation occurs all over the world for prostate cancer rates due to differences in detection practices, treatment, lifestyle factors such as western diet (fat items and dairy products) and genetic factors (Center et al., 2012).

Family history of prostate cancer

Several studies have consistently indicated familial aggregation of prostate cancer risk, showing 2 to 3 fold increased risk of prostate cancer among male persons who have a first-degree relative (father, son, brother) with a positive history of prostate cancer (Stanford & Ostrander., 2001). Bashir et al (2014) investigated that family history of prostate cancer was strongly associated with increased risk of prostate cancer (OR: 7.324, 95% CI: 1.798-29.841). Nemesure et al. (2012) found in their study that men whose fathers or brothers were patient of prostate cancer had 3

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Table 1. SEER Incidence and U. S. Mortality Age Adjusted Rates by Race (2007-2011)

Race/ Ethnicity	Incidence Rates per 100,000 persons	U. S. Mortality Rates per 100,000 person
All Races	147.8	22.3
White	139.9	20.6
White Hispanic	120.3	19.1
White Non-Hispanic	143.3	20.7
Hispanic	121.8	18.5
Black	223.9	48.9
Asian/ Pacific Islander	79.3	10
American Indian	71.5	16.8

*Adapted from Howlader et al., 2014

Table 2. Relative Risk (RR) and 95% Confidence interval Related to Family History of Prostate Cancer

Risk Group	RR for Prostate cancer (95% CI)
Father having prostate cancer	2.35 (2.02-2.72)
Brother(s) having prostate cancer	3.14 (2.37-4.15)
One affected FDR	2.48 (2.25-2.74)
Affected FDR diagnosed < 65 years of age	2.87 (2.21-3.74)
Affected FDR diagnosed at the age of 65 years or more	1.92 (1.49-2.47)
Affected second degree relative	2.52 (0.99-6.46)
Two or more affected FDR	4.39 (2.61-7.39)

times higher risk of developing this disease as compared to without family history. In addition, men having affected two or more first degree relatives of prostate cancer had almost 5 times higher risk of developing the disease. The majority (64%) of early onset prostate cancer cases reported a family history of this disease and more than 40% having a confirmed first degree affected relatives of prostate cancer (Lange et al., 2012). Zeegers et al. (2003) conducted a meta-analysis based on 33 epidemiologic studies. They found that the risk of developing prostate cancer was almost three times higher for men with affected brothers and father of prostate cancer. A meta-analysis of 33 epidemiologic studies has provided more detailed information about risk ratios associated with family history of prostate cancer. More risk was found for men with affected brothers as compared to men with affected fathers in this meta-analysis. However the cause for this difference in risk is unknown. Furthermore, risk was increased with increasing number of affected first-degree relative (FDR). Table 2 shows the summary of Relative Risk related to a family history of prostate cancer of above meta-analysis (Kiciński et al., 2011).

Diet

The Western lifestyle, particularly more consumption of fat, red meat and dairy products may be responsible for developing the higher prostate cancer risk. In a multiethnic study of dietary factors, risk of prostate cancer was positively associated with total fat intake in whites, Asian Americans and African Americans (Whittemore et al., 1995). More consumption of fat items, especially red meat and dairy products was directly related to prostate cancer risk in many studies (Vlajinac et al., 2010; Hardin et al., 2011). Mahmood et al. (2012) investigated that the risk of developing prostate cancer was almost 12 times higher with more consumption of red meat and dairy products. Song et al. (2013) found in their study that more consumption of whole milk was positively associated with fatal prostate cancer and worse survival in older age. Joshi et al. (2012) investigated that more consumption of red meat cooked at high temperature was positively associated with the development of advanced prostate cancer. Bashir and Malik (2015) recently found in their study in Pakistan that consumption of red meat and use of fat items were strongly associated with increased risk of prostate cancer (OR: 3.413, 95% CI: 1.464-7.959) and (OR: 2.454, 95% CI: 1.171-5.145), respectively.

Obesity

Obesity is measured by body mass index (BMI). It is calculated on the basis of weight in kg divided by the square of height in meters, (kg/m^2). A person is considered to be obese if its BMI is greater than or equal to 25(Anuurad et al., 2003). Although the findings on obesity are mixed, but recent studies suggest that obesity is consistently related to aggressive prostate cancer (Hsing et al., 2000). The risk of prostate cancer was almost 2 times higher in case of obese men (Ganesh et al., 2011). Obese men had almost six-fold higher risk of developing prostate cancer as compared to non-obese having odds ratio and 95% confidence interval 5.793 and 2.668-12.579, respectively (Bashir et al., 2014).

Sexual behavior and Sexually transmitted diseases

Numerous case-control studies reported a positive association between prostate cancer risk and history of sexually transmitted diseases (gonorrhea and syphilis) (Dennis and Dawson, 2002). History of prostatitis (OR 25.0, 95% CI 9.2-67.9) was observed to be positively associated with prostate cancer risk (Hosseini et al., 2010). On the other hand many prospective studies have not shown any significant association between history of gonorrhea or syphilis and prostate cancer (Huang et al., 2008; Sutcliffe et al., 2006). In different studies, the frequency of sexual activity has been found to have direct relationship with the development of prostate cancer. A meta-analysis conducted by (Dennis and Dawson, 2002) concluded from 12 retrospective studies that increased sexual frequency (three times per week) may be associated with an increased risk of prostate cancer (OR: 1.2, 95% CI: 1.1-1.3). Pourmand et al (2007) observed in their study that the risk of prostate cancer was increased with two or more than two times sexual intercourse per week (OR: 3.14, 95% CI: 1.2-8.2).

Occupation

Occupation is highly correlated with prostate cancer risk in many studies. A Meta-analysis was conducted by

Ragin et al. (2012) to investigate the effect of farming and pesticides used on prostate cancer. The study was based on 3978 confirmed cases of prostate cancer and 7393 controls. It was found that farmers had about four times more risk of prostate cancer as compared to controls. Meyer et al. (2007) found in their study that farmers, who applied pesticides, had almost 2 times higher risk of developing prostate cancer. Parent et al (2009) conducted a case control study to evaluate the relationship between prostate cancer and exposure of different agricultural chemicals, i.e. pesticides, acetic acid, arsenic compounds, polycyclic aromatic, gasoline & diesel engine emission, mono nuclear aromatic hydrocarbons, lubricating oils and greases, alkanes with ≥18 carbons and solvents. Results revealed that there was twofold risk of developing prostate cancer among farmers with exposed to use of pesticides as compared to un-exposed farmers. Furthermore farmers, who exposed to diesel engine emission, had almost 6 times higher risk of developing this disease.

Smoking

The effects of smoking on the epidemiology of prostate cancer are inconclusive. Generally smoking has not been considered a risk factor for prostate cancer. Though, a meta-analysis of 24 cohort studies reported a significant increase in prostate cancer risk for heavy smokers (RR: 1.22, 95% CI: 1.01-1.46) (Huncharek et al., 2010). Current and past smokers had higher risk for prostate cancer, but the association was statistically significant only in case of past smokers (Tyagi et al., 2010). Furthermore, smoking is positively associated with prostate cancer mortality. Smokers have 14% more risk of dying from prostate cancer as compared to nonsmokers (Huncharek et al., 2010). Smoking may stimulate the development of more aggressive, hormone-sensitive cancers through several mechanisms, comprising effects on sex steroid hormone levels and continuous exposure to carcinogens for example polycyclic aromatic hydrocarbons contained in cigarette smoke (Zu and Giovannucci, 2009).

Protective Factors

Several studies suggest that consumption of vegetables and fruit are associated with a lower risk of developing prostate cancer (Liu et al., 2012; Zhou et al., 2013). Askari et al. (2014) conducted a case-control study to evaluate the association between consumption of vegetables and fruit and prostate cancer. They found a significantly reduced risk of prostate cancer for intake of vegetables and fruit (OR: 0.31, CI: 0.02-0.21) and (OR: 0.30, CI: 0.06-0.40) respectively. Tomato and tomato sauce were inversely associated with prostate cancer risk having odds ratio and 95% confidence interval 0.05 and 0.01-0.40 respectively (Mazdak et al., 2012).

Some studies suggest that selenium, an important trace element found in fish and grains was inversely associated with prostate cancer risk (Vogt et al., 2003). Better lifestyle (physical activity & moderate exercise) was also observed to be negatively associated with prostate cancer risk (Hosseini et al., 2010; Bashir et al., 2014).

Finally, male persons with diabetes mellitus appear to have lower risk of developing prostate cancer. Turner et al (2011) conducted a case-control study in England to evaluate the association between diabetes mellitus and prostate cancer risk. They investigated that diabetes was associated with a reduced risk of prostate cancer having odds ratios and 95% confidence interval (OR: 0.78, CI: 0.61-0.99), respectively. A prospective analysis of 5 ethnic populations was conducted by Kevin et al. (2009), investigated that diabetes was associated with a 20% lower risk of developing prostate cancer. This inverse association was seen in all racial populations. A large number of epidemiologic studies provide strong support that type-2 diabetics decreased the risk of prostate cancer (Pierce, 2012).

Trends in Incidence and Mortality

Worldwide, incidence rates have been increased considerably through early 1990's when screening with prostate specific antigen (PSA) was introduced (Hsing et al., 2006). Prostate cancer incidence rates varies more than 25-fold worldwide, the rates are highest in New Zealand/ Australia and Northern America (111.6 and 97.2 per 100,000 men, respectively), and in Northern and Western Europe, because prostate specific antigen (PSA) testing and biopsy has become widespread in these areas. Incidence rates are also comparatively high in some less developed regions such as the Caribbean, Southern Africa and South America (79.8, 61.8 and 60.1, respectively), but low in Asian populations with estimated rates of 10.5 in Eastern Asia and 4.5 per 100,000 men in South-Central Asia. These rates are based upon the cases of prostate cancer worldwide in 2012 (Ferlay et al., 2015). Prostate cancer is very common in some of the Indian registries, but at the country level incidence rates were very low, such as 6.9 in Mumbai, 5.3 in Kolkata and 3.0 in Nagpur (Moore et al., 2009). Prostate cancer is the common most malignancy among men in Pakistan. It is one of the third leading sites of tumors in men with a ratio of almost 7% of all malignancies (Ahmad et al., 2009). The age standardized incidence rate during 1998-2002 in Karachi (Pakistan) was 10.1 per 100,000 men (Bhurgri et al., 2009). This is almost similar to Asia- Pacific region 9.9 per 100,000 men but significantly lower than the whole world 32.8 per 100,000 men (Baade et al., 2013). Some studies reporting that Asians living in the United States have greater incidence rates of developing prostate cancer than the average rates of Asians living in their native states, yet incidence rates among Asian Americans are still much lower than white Americans (McCracken et al., 2007).

There is less variation in mortality rates ten-fold worldwide (almost 3 to 30 per 100,000 men) as compared to incidence rates. Mortality rates are generally high in black populations such as Caribbean and sub-Saharan Africa (29 and 19-24 per 100,000 men) and very low in South-Central Asia (2.9 per 100,000) and intermediate in the Oceania and Americas (Ferlay et al., 2015). Table 3 shows the number of new cases and deaths per 100,000 people (all races) during 2001 and 2011 (Howlader et al., 2014).

Table 3. Number of New Cases and Deaths Per 100,000 People (All Races, Males), Age-Adjusted

Year	New Cases-SEER 9	New Cases-SEER 13	Deaths-US
2001	185	180	29.5
2002	182.2	177.8	28.7
2003	169.6	165.3	27.2
2004	165.8	165.3	26.2
2005	156.7	153.9	25.4
2006	171.8	164.3	24.2
2007	174.6	167.5	24.2
2008	157.5	152.8	23
2009	154.4	149.4	22.1
2010	146.7	141.7	21.8
2011	139.9	135.4	20.8

Survival

Prostate cancer patients have a good survival rate if the cancer is diagnosed at an early stage (Leitzmann and Rohrmann, 2012). To get 5-year survival rates, consultants have to look at persons who were treated at least 5 years ago. Improvements in detection and treatment recently may result in a better outlook for men now being diagnosed with prostate cancer. 5-years relative survival rate for local and regional stage are almost 100% and for distant stage is 28% (American cancer Society, 2015). Survival in Indian population was 49% for localized disease, 24% for direct extension and regional node involvement and 13% for metastatic patients (Yeole and Sunny, 2001). Survival of cancer patients tends to be very poorer in developing countries, due to diagnosis at a late stage and inadequate facilities of treatment (Jemal et al., 2011).

Advanced Stage

Generally the patients contact the doctors when the malignancy almost spread in other parts of body. This is an advanced stage of cancer which is called Metastatic disease. The malady at this stage is incurable and causes significant mortality. Average survival at this stage is almost 3 years, but in some cases may be longer. Symptoms of advanced prostate cancer are bone pain, spinal cord compression, fatigue, depression, obstruction, weight loss, constipation and anemia. Bone disease is very common in 90% of the metastatic patients. At this virulent phase, the efforts should be made to sustain the quality of life with the help of palliative care. Through palliative care the patients suffering from advanced stage of this disease are treated, physically, spiritually, socially and psychologically (Thompson et al., 2007).

Summary

Prostate cancer is characterized by wide variations in incidence and mortality in the world, combined with evidence of an increasing load of incidence in several areas. Epidemiologic observations provide vital clues to the etiology of prostate cancer. No doubt, the causes of prostate cancer are not still clear but epidemiologic studies have brought out various intriguing leads, including environmental as well as genetic factors. With the help of freshly available tools in molecular biology and genomics, investigation of the individual as well as combined effects of these factors have been started by a new generation of large-scale population-based studies. These studies may provide tangible evidence for risk factors which may be helpful in identifying subsets of the population which are more capable of getting prostate cancer.

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