## MINI-REVIEW

# **Epidemiology, Etiology, Diagnosis and Treatment of Prostate Cancer**

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#### Abstract

Prostate cancer is more common in men over the age of 65 years. There are 15% cases with positive family history of prostate cancer Worldwide. Prostate cancer is the second leading cause of death among the U.S. men. Prostate cancer incidence is strongly related to age with the highest rates in older man. Globally millions of people are suffering from this disease. This study aims to provide awareness about prostate cancer as well as an updated knowledge about the epidemiology, etiology, diagnosis and treatment of prostate cancer.

Keywords: Prostate cancer - etiology - epidemiology in worldwide prevalence - treatment - literature review Pakistan

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#### Introduction

Prostate gland is the male sexual gland which is present in front of the rectum and between the bladder and penis (Seisen et al., 2012). Prostate cancer is the malignant cancer and second most frequent malignancy in men (second to skin cancer). Although the disease is present in many patients but it is not causing any problem and will not responsible for their death. According to one study, incidence of prostate cancer in Iranian population is more as compared to other areas of Asia (Akbari et al., 2008).

Age is the major risk factor but there is also an increased risk in those with a family history of either prostatic or breast cancer. Median age is 72 years (Vinjamoori et al., 2012). African Americans have an increased risk of disease as well as increased rates of advanced disease (Julie et al., 2009). In UK 36% of cases were diagnosed in men aged 75 years and only 1% were diagnosed in the under 50s. Asian Americans are affected less common as compared to others.

It is 2 to 3 times more in person whose brother or father has prostate cancer as compared to those who have no family history of prostate cancer. If a person has three immediate family members suffering from prostate cancer then there is 10 times more chance of prostate cancer as compared to person that has no family history of prostate cancer. High fat diet also increases the chance of prostate cancer.

Patients may be asymptomatic but the commonest complaint is difficulty with micturition, straining to start, frequency, and nocturia. All these can arise from benign prostatic hypertrophy as well as malignancy. Obstructive voiding symptoms are most often due to benign prostatic hyperplasia which occurs in the same age group. Malignant changes occur in prostate cells that further proceed toward carcinoma. Environmental and genetic influences cause promotional proceedings and sequence of commencement.

As the axial skeleton is the most common site of metastasis patients may present with back pain or pathologic fractures. Prostate cancer incidence in the United States increased steadily throughout the second half of the 20th century. This increase appears related to the increase in life expectancy and associated increase in number of older men at risk for prostate cancer. The incidence of cancer increases with age. A 50 years old American man has a lifetime risk of 40% for latent cancer, 16% for developing clinically apparent cancer and a 2.9% risk of death due to prostate cancer. Other factors including widespread use of prostate specific antigen (PSA) screening also appear to have contributed to the increase in annual prostate cancer incidence (Verim et al., 2013). PSA is a glycoprotein produced by cell, either benign or malignant of the prostate gland. PSA screening identified a large number of prevalent cases of asymptomatic prostate cancer. People suffer from prostate cancer at 65 years of age. Prostate cancer causes 41000 deaths in America annually.

Currently most prostate cancers are associated with palpably normal prostates and are detected on the basis of elevation in serum PSA. The annual incidence of prostate cancer peaked at 350,000 cases in 1993. After declining

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in the late 1990s, the annual incidence of prostate cancer is rising again. Receptors for vitamin D 3 are found on human prostate gland. Vitamin D 3 increases apoptosis and differentiation and decreases metastasis, invasiveness and proliferation. In failure of androgen deprivation, second line therapy may be vitamin D. Risk of prostate cancer increases in poor sun exposure or vitamin D deficiency in early age (Chen and Holick, 2003).

Measurement of serum PSA is useful in detecting and staging prostate cancer, monitoring response to treatment and detecting recurrence before it becomes clinically evident. In contrast to the striking variations in annual rates of prostate cancer diagnosis, prostate cancer mortality rates have declined steadily since 1990. Prostate cancer preferentially spreads to regional lymph nodes and bone. Significant metastases to lung liver or other visceral organs are less common.

#### Epidemiology

This is the second commonest cancer in males, particularly affecting older men: over 80% of cases are diagnosed after age 65. Despite this, only 10% of men with prostate cancer die of the disease. This is the paradox of prostatic cancer: autopsy examination of men aged 70-79 reveals prostate cancer in 39% and this increases to 43% in those aged 80. Kang et al, reported that American have less severe characteristics than Korean prostate cancer patients (Kang et al., 2013). Increased incidence, disease burden and fatality make the cancer a global health problem. In the United States, there were approximately 234,460 new prostate cancer cases and 27,350 deaths in 2006 (Matthew et al., 2006). Belbase et al reported that 31 (18.23%) people were with prostate cancer out of 170 cases of malignancies of genitourinary tract (Belbase et al., 2013). In Iran, incidence of prostate cancer is 9.6 per 100, 000 (Talaiezadeh et al., 2013). Incidence and mortality rates for prostate cancer are highly variable worldwide. In the United Kingdom, second most cancerous disease in men is prostatic cancer. In the United Kingdom, each year, 35000 men are diagnosed with prostate cancer and 10,000 patient die with prostate cancer.

Prostate cancer is more common in men above 50 years of age. Sixteen percent of male in American are diagnosed as having prostate cancer and 3rd percent die from prostate cancer. It occurs most common in 50 years of age African-American are more affected from this disease. Native American and hisponics also suffer from this disease.

In the Western World, most common cause of cancer mortality is prostate cancer. In 2012, 241, 740 cases of prostate cancer were diagnosed according to American cancer society. American cancer society reported 29% new cases in 2012. American cancer society reported that 28, 170 men died in 2012 due to prostate cancer. Advanced disease was reported in 4% of patients. In Asia, incidence of prostate cancer and mortality rate has increased (Moore et al., 2010). Study shows that Korean people have worse disease than American people (Kang et al., 2013). Initial treatment of prostate cancer is androgen deprivation (Zhi et al., 2014). According to one study, incidence of prostate cancer is increased and is estimated that new cases will be 78,468 in 2020 (Harutake et al., 2014).

#### Etiology

A high intake of calcium is considered to be cause of prostate cancer. Dairy products contain high amount of calcium. Increase calcium level decreases the concentration of 1, 25-dihydroxyvitamin. Vitamin D is considered to protect prostate cancer. A study conducted to investigate the association of calcium intake, dairy product and risk of prostate cancer showed there is greater risk of prostate cancer in person taking high calcium intake and dairy products. Total number of persons investigated was 20885, in which 1012 were documented to be suffering from prostate cancer. There was more consumption of calcium and dairy products in patient with prostate cancer (Chan et al., 2001). Unlike breast cancer the presence of either estrogen or progesterone receptors does not relate to endocrine responsiveness. Meat and dairy product are the main cause of prostate cancer. Prostate cancer risk increases by increased level of insulin like growth factor in circulation.

#### Diagnosis

Androgen induces the production of a prostatic secretory glycoprotein, prostate-specific antigen that can be used with caution to screen for disease and monitor response. Both of these markers are not specific to malignancy and will be elevated after manipulation of the prostate by digital examination. If the disease is confirmed histologically other tests include transrectal ultrasound, radioisotopic bone scan In-capromab pendetide (Protascint scan). The latter test uses antibodies to PSA, linked to in order to determine whether there has been spread to the lymph nodes. Patients in urinary retention or those with urethral obstruction due to regionally advanced prostate cancers may present with elevation in blood urea nitrogen or creatinine. The diagnosis is based on digital rectal examination and core needle biopsy. Various grading tests for prostatic cancer have been devised but that in most widespread use is the Gleason system (Gleason et al., 1974). Approximately 98% of patients with metastatic prostate cancer will have elevated PSA (Anderson-Jackson et al., 2012). However there are rare cancers that are localized despite substantial elevations in PSA. Prostate specific antigen increases in enlarged prostate gland, older age, prostatitis, ejaculation, riding a bicycle, certain urologic conditions and certain medications (Zheng et al., 2012). Prostate specific antigen decreases in 5- alpha reductase inhibitors, herbal mixtures, obesity, aspirin use, thiazide diuretic, statin. Patients with intermediate levels of PSA usually have localized and therefore potentially curable cancers. It should be remembered that approximately 20% of patients who develop radical prostatectomy for localized prostate cancer have normal levels of PSA (Nath et al., 2012). Prostate biopsy specimens are from the apex, mid portion and base in men who have an abnormal DRE or an elevated serum PSA, or both (Hayes and Barry, 2014). Extended pattern biopsies,

including a total of at least ten biopsies are associated with improved cancer detection and risk stratification of patients with newly diagnosed disease.

### Treatment

Healthy diet and foods are fruits and vegetables. These are rich in flavonoids, fibers, vitamin C and carotenoids (Garg et al, 2014). Mortality and incidence rate of prostate decreases by dietary measures. Development of cancer slowed or prevented by use of fruit and vegetables. Plants contains various anticarcingenic substances as isothiocyanates, isoflavones, dithiolthiones, carotenoids and vitamin E. Studies have been conducted to investigate the association of diet with prostate cancers but results are inconsistent (Meng et al., 2013). Vegetarians are at decreased risk and vitamins A and E may have a protective effect (Klein et al., 2011). Many prostate tumors are hormone sensitive and the presence of dihydrotestosterone receptor is associated with response to androgen deprivation (Titus et al., 2005). Physical activity, dietary supplements and dietary factor may be helpful in prevention of prostate cancer. Selenium and vitamin E decreases the risk of prostate cancer (Wolk, 2005). The surgery aims to remove prostate, seminal vesicles, ampullae of vasa deferentia, and achieve tumour-free margins but this is not achieved in over 25% of cases. Radical prostatectomy is carried out but complications are observed such as impotence and urinary incontinence in up to 20% of cases. In a large series of 1153 patients treated by radical prostatectomy at the Mayo Clinic the 10 year survival was 75% with only 10% of cases dying of metastatic disease (Zincke et al., 1994). Finasteride can prevent the prostate cancer or decrease the risk of death.

## **Clinical Implications in Asian Countries**

Prevalence and mortality due to prostate cancer has gradually increased in Asian populations (Nath et al. 2012). Prostate cancer occurs most commonly in old age. There is strong relation of prostate cancer with increasing age. Most of patients with prostate cancer are above age of 65 years and prostate cancer increases two fold after seventy years of age in Asian countries. Sedentary lifestyle, environmental carcinogens, family history of prostate cancer, endogenous factors and oxidative stress associated with aging process predisposes subjects to develop the prostate cancer (Bhurgri et al. 2009). Prevalence of prostate cancer is less in Asian countries than European Caucasians and African American. Demographics and clinical variables both are used to diagnose the prostate cancer, most common malignant tumor. A study indicated that prevalence of prostate cancer was less in European countries and North America than Asian immigrants (Visser and Leeuwen, 2004). Lacey et al, reported that physical activity has protective role in cancer prevention. Physical activity enhances immune mechanism, reduces obesity and reduces testosterone level that collectively contributes toward prevention of prostate cancer. This protective role of physical activity was demonstrated in Chinese population. Study showed that incidence of

prostate cancer was less in subjects exercising once a week than persons with sedentary lifestyle (Lacey et al. 2001). Quan et al conducted a study to investigate the military men for prostate cancer. Patient with prostate cancer were 5% from Asia while total men in military from Asia were only 3.4% (Raymundo et al., 2010). Prostate cancer is the most common disease in men in Asia. Religion affiliation, economics, values and cultural norms influence the dietary decision. Lifestyle is based on education, disease and health status, income level, social class and area of residence is base for dietary pattern. In Asian countries, dietary pattern differs between urban and rural areas. For example, beef is consumed more in areas of Pushtun belt in Pakistan. Fruit and vegetable consumption also vary in different regions of Asia. In Asian, countries, prostate cancer occurs in subject consuming fats and red meat and relation of prostate cancer with white meat is less significant in Pakistan. Consumption of vegetables provides protection against prostate cancer (Hsing et al. 2002). Rural living, forming, consumption of red meat, previous smoking, family history of prostate cancer, height and age are strongly associated with prostate cancer in Pakistan. Mixing of meat and vegetables may provide protective role in cancer prevention in Asian countries.

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