Review Article

Socio-demographic and Lifestyle Factors Related with the Risk of Prostate Cancer

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Abstract: Carcinoma of prostate is the most frequently diagnosed cancer among men in developed countries. Incidence rate among African-Americans is highest (185.4 per 100,000) in the world followed by Caucasian-Americans (107.8 per 100,000). Despite high morbidity and mortality, etiology of prostate cancer remains largely unknown. Advancing age, race and family history are the only established risk factors. However, racial and genetic factors alone cannot explain the wide international variation in disease distribution. The objective of this review was to summarize socio-demographic and lifestyle factors in relation to prostate cancer risk. A systematic search was conducted including articles published in peer reviewed journals indexed in MEDLINE/ Pub Med database. Prostate cancer incidence was found to be proportional to increasing urbanization and rise in socioeconomic status. Factors associated with increased prostate cancer risk include raised androgens levels, high saturated fat in diet, reduced physical activity, obesity, smoking and working as farmer. Pattern of prostate cancer incidence and mortality suggests that both genetic and environmental factors contribute towards an excess risk of disease; nevertheless, environmental and life-style factors, especially trend of urbanization and change in socioeconomic status may have accrued the prostate cancer risk in developing countries.

Keywords: Prostate, Cancer, lifestyle, social, demography, risk, review, literature, urbanization.

Introduction

Prostate is a glandular structure forming part of male reproductive system. It is a retro-peritoneal organ located immediately beneath the urinary bladder, encircling its neck, above the urogenital diaphragm, penetrated by proximal part of urethra. In normal adult men, it is roughly the size and shape of chestnut, weighs approximately 20 grams and is devoid of a distinct capsule.[1] Histologically, it is a compound tubulo-alveolar gland consisting of ducts and acini.

Prostate gland is an endocrine-dependent organ that secretes a thin, milky fluid which contains citrate, calcium, phosphate, a clotting enzyme and pro-fibrinolysin. Growth of prostate is governed by many local and systemic hormones, whose exact function is still unknown.[2]

Main hormone acting on prostate is testosterone which is secreted by leydig cells of testes controlled by luteinizing hormone of anterior pituitary. Testosterone is converted to 5-dihydrotestosterone by 5-α reductase enzyme found in high concentration inside prostate gland.[3]

Three pathologic processes that affect prostate gland include inflammation, benign nodular enlargement and tumors. Benign prostatic hypertrophy (BPH) is the most common condition that occurs with advancing age. Prostate cancer shares a number of features with BPH and intra-epithelial neoplasia (PIN) a putative precursor of prostate cancer. There has been a suggestion by some experts that nodular hyperplasia of the prostate can lead to prostate cancer; however universal acceptance of this suggestion is lacking and any concurrence of these two conditions could be due to their relationship with aging.[4] On the other hand, the continuum that culminates in high-grade PIN and early invasive cancer is characterized by progressive basal cell layer disruption, abnormalities in markers of secretary differentiation, increasing nuclear and nucleolar alterations, rising cell proliferation, variation in DNA content and higher genetic instability.

Carcinomatous lesions occur mostly in posterior location morphologically and are multifocal. Histologically, most lesions are adenocarcinoma which produce well-defined gland pattern. On the other hand, epidermoid carcinoma, adenoid cystic carcinoma and transitional cell carcinoma are rare forms of prostatic cancer.[5] Degree of glandular differentiation and growth pattern of tumor in relation to the stroma has been graded using many grading and staging protocols. Among them Gleason system is the most frequently used classification system.[6]

1. Historical Perspective

Earliest reference about urinary tract obstruction by

B.C) defined several types of cancers including stomach, breast and prostate; coined the term" Karakinos" meaning hard lump for these manifestations. Galen, the Roman physician around 160 A.D developed his humoral theory to explain the etiology of cancers and his views dominated the field of medicine for next 1500 years.[7] Role of prostate cancer in causing bladder outlet obstruction was first described by Antonio Ferri of Naples in 1530 and by anatomist Niccolo Massa in 1536. Vesalius produced the first anatomical drawings of prostate gland eight years later. In good old times, prostate cancer was considered rare disease owing to shorter life expectancy of individuals and poor detection methods. In 1649, Riolan described and reported the first prostate tumor cancer in literature. An English anatomist and surgeon John Hunter in 1786 demonstrated that growth of prostate in male animals could be prevented by removal of testicles.[8] Surgical and medical treatment of prostate cancer initiated in early nineteen century, when Theodor Billroth first did perineal prostatectomy in 1867, and Hugh Young of John Hopkins University extended the surgical techniques to be later called as Radical Perineal Prostatectomy which remained the treatment of choice until 1940's. During the thirties, Edith Spoul, Alexander Gutman and Ethel Benedits of Presbyterian Hospital in New York reported an elevated acid phosphatase among cases of prostate cancer with bone metastasis. They also demonstrated that blood levels of these phosphates correlated with prognosis of the disease.[9] In 1941, Charles Huggins used estrogen to oppose testosterone production in men with metastatic prostate cancer and was awarded Nobel Prize in medicine for this discovery.[10]

In early fifties, first trials on external radiotherapy were initiated and during sixties, it became an important tool in fight against this slow progressing tumor. Furthermore, several chemotherapeutic protocols were also developed in 70's and 80's by Gerald Murphy of National prostate cancer project in United States using Cyclophosphamide, 5-fluro-uracil, Semustine and Streptozocin.[11] Evidence to support the relationship between prostate cancer and environmental conditions, lifestyle patterns and dietary habits emerged in late nineties and Prostate Specific Antigen (PSA) test was introduced for screening high risk populations.[12] Since that time, growing research projects are now targeted on early identification of modifiable factors associated with the development of this debilitating cancer and adopting primary prevention strategies.

2. Lifestyle and Its Relationship With Disease Development

The word 'lifestyle' was originally coined by an Austrian Psychologist Alfred Adler in 1929; however its use in broader sense only dates back since 1960's. In sociological perspective, lifestyle is the way a person lives or manner of living of a particular person, group or culture.[13] It is the set of behaviors that makes sense to both others and oneself in a given time & space, including social relations, consumption, entertainment, dress and diet. Practices and behaviors within lifestyle are mixture of habits, ways of doing things and reasoned actions. A lifestyle also reflects an individual's attitude and values.

Lifestyle related diseases are sometimes called the diseases of civilization or longevity, since these appear to increase in frequency in countries which are more industrialized and with rise in life expectancy. Some of these conditions include Alzheimer's disease, asthma, type 2 diabetes mellitus, obesity, metabolic syndrome, cancers and heart diseases.[14] Lifestyle factors attributed to the development of these conditions consist of change in dietary habits, reduction in physical activities, smoking tobacco and increased alcohol consumption.[15] Migrant studies have also provided a strong evidence to support the argument that environmental factors in addition to genetic factors are being increasingly identified as the risk factor in case of prostate cancer worldwide.[8]

3. Global Burden of Prostate Cancer

With an estimated worldwide incidence of 25.3 per 100,000 men and mortality of 8.1 per 100,000 men, prostate cancer is the most common cancer among males now.[2] It is the third leading cause of cancer in Western Europe and North America. Global burden has increased in last 30 years. Incidence is highest in black American men, intermediate in white men and lowest in Chinese and Asian men. It is estimated that slightly over 100,000 new cases are detected every year, of which one third prove to be fatal.[4] More than ninety-five percent of prostate cancers are adeno-carcinoma.[1] Despite a considerable international variation in incidence of clinically detectable prostate cancer, the prevalence of latent cancer at autopsy is constant across countries and ethnic groups. This variation may be due to differences in detection methods, quality of registration systems, actual difference in underlying risk or biological behavior of resultant tumors. Differences in procedures to detect prostate cancer early, based on specimens obtained through trans-urethral resection of prostate (TURP)

in eighties and introduction of prostate specific antigen (PSA) testing during nineties might result in increased incidence rate in developed countries and may be due to lead time bias. [5]

4. Established Risk Factors

4.1: Effect of Aging

Aging is the most important single factor for occurrence of prostate cancer. This carcinomatous disease is almost unknown before the age of 40 years, however, from fifth decade onward, frequent microscopic foci of carcinomatous change have been found at autopsies of men.[16] A large number of men are diagnosed when they are around 60-70 years. Moreover, older men are more likely to be diagnosed with aggressive form of disease and thus lower survival. Essentially, all men with circulating androgens will develop microscopic prostate cancer if they live long enough. This extraordinary linkage with age suggests that prostate cancer results from accumulation of genetic damage, perhaps due to oxidative stress or other endogenous or exogenous factors. Incidence of prostate cancer increases exponentially with advancing age. Surveillance Epidemiology and End Results (SEER) program estimates from 1996-2000 indicated that prostate cancer incidence is almost 18 times higher among US individuals over the age of 65 than the persons below this age.[17]

4.2 Genetic Factors and Racial/Ethnic Variation

Higher burden of disease among African-American (risk is 60 times higher than a Chinese man living in Shanghai China) and a great degree of international variation in other continents points to this important factor in the aetiology.[6] Racial and ethnic differences in incidence have thought to be environmental rather than genetic since Japanese and Chinese migrants having low risk in home countries have shown a rapid rise in risk when living in more industrialized countries. Despite this consistent observation, extent of contribution of ethnicity and racial variation is still inadequately 'understood'.

A number of familial aggregation studies have consistently suggested that a man having the history of prostate cancer in family (first degree relatives-father, son, brother) has twice to thrice times higher risk to develop adenocarcinoma of prostate.[18] It has been postulated that genetic factors interact with environmental exposures to raise the susceptibility of men with advancing age. Furthermore, a recent study involving twins has reported that at least 42% (95% CI 29-50) of the variation may be attributed to genetic factors.[19] In addition, segregation and linkage analyses have shown that prostate cancer may be inherited as autosomal dominant pattern. High-penetrance genes (HPC1, HPC2, HPCX, CAPB, and PCAP at 8p22-23) are responsible for only 10% of all prostate cancer.[20] Studies are still searching the possibility of genetic link in relation to androgen biosynthesis, identifying the genes associated with insulin-like growth factors for probable relationship with prostate cancer and exploring gene encoding enzymes that metabolize carcinogens and other toxins.[21]

Furthermore, it has been observed that in certain individuals, there is a genetic susceptibility to alter the function of cytochrome p450. These individuals take high concentration of cruciferous vegetables (cabbage, broccoli, cauliflower, radish), which contain vitamin C, soluble fibres and selenium, presence of which might decrease the risk of prostate cancer.[22] Some studies with large sample size have demonstrated no association in this regard. A recently discovered compound in Brassica vegetable family, di-indolyl-methane, has stated to be a strong androgen receptor antagonist in human prostate cancer cells.[23]

4.3: Role of Androgens and Growth Factors

Androgens play a key role in development and mainte- nance of the prostate cancer. This disease is found to be absent in castrated men. Increased serum level of androgens has reported to be associated with higher risk of prostate cancer; however the precise mechanisms by which these androgens play the role is still unclear. Furthermore, animal studies have shown that administration of testosterone in rats induces prostate cancer.[24] It has been postulated that testo-sterone plays a substantial role in either triggering the prostate cell growth or at least function as tumour promoter. Vitamin D has also reported to be protective against prostate cancer since it has potent anti-proliferative effect on prostate cells; however the results from epidemiological studies are inconsistent. In addition to above mentioned factors, recently another growth factor called insulin like growth factor (IGF-1) has been linked to increase the risk of prostate cancer. IGF-1 and IGF-2 are polypeptides that function as both tissue growth factors and endocrine hormones with mitogenic effect on prostate gland cells. The effect of IGF-1 is also more marked in aggressive form of disease. [25]

5. Probable Risk Factors

5.1: Dietary Factors

A wide variety of food elements in diet have been

studied in relation to the risk of prostate cancer using descriptive and ecological study designs; however, most of these investigations were conducted on populations living in developed countries. There has been somewhat consistent observation that consumption of animal fat and red meat is found more commonly among prostate cancer cases. Mechanism by which fats contribute in cancer initiation or promotion is not clear, but fat induced oxidative stress may be involved in this process. Despite positive association about the role of saturated fats in prostate cancer development presented by four case control studies, one large cohort study reported an inverse association (RR: 0.78, 95% CI: 0.56-1.10), though this relationship was not statistically significant.[26] A positive association was also observed for dietary linolenic acid (RR. 3.43; 95% CI. 1.67-7.04). Chronic excess of zinc may be associated with prostate cancer risk, although in vitro studies suggested opposition action.[27]

Some studies have implicated the use of dairy items like milk products in relation to prostate cancer risk. It is suggested that rising amount of calcium in dairy products may be associated with increased risk; whereas men who consume low calcium and high phosphorus had an RR of 0.6 (95% CI.0.3-1.0).[28] Furthermore, increased consumption of tomato, pink guava, pink grapefruits, water melons, Papaya (containing lycopene), cruciferous vegetables (cabbage, cauliflower), fish, Alliums vegetables (onions, garlic) and foods containing selenium, vitamin E have shown to decrease the risk of prostate cancer, although the results are inconsistent.[29]

5.2: Occupations

Epidemiological studies are consistently documenting that farmers have around 10% excess risk of developing prostate cancer. This may be due to exposure of insecticides and pesticides which contain organo-chloride compounds which in turn can affect circulating hormones; however epidemiological evidence linking any chemical in this regard is missing. Furthermore, exposure to cadmium is associated with an increased risk of prostate cancer.[16] Moreover, workers in heavy metal and rubber industry may have an increased risk, suggesting the need to explore the exposure of various chemicals in different occupations. A recent case control study in Germany found an association between diesel fuel exposure and prostate cancer risk (OR 3.7; 95% CI. 1.40-9.8).[30]

5.3: Energy Intake and Obesity

Abdominal obesity has been reported to be associated with increased risk of prostate cancer. This can be explained on the basis that there may be alteration in hormone synthesis or metabolisms, which might have a role in the etiology. Recent data indicates that obesity is more consistently associated with aggressive form of prostate cancer. Elevated body mass index was associated with 4.5 times higher risk of prostate cancer in a case-control study conducted in Italy.[31] Similarly a study in France suggested that obese men had 2.5 times the risk of developing the prostate cancer. There has been observed a positive association with high energy intake and risk of prostate cancer among Swedish (RR.1.70; 95% CI. 1.10-2.61); however, the study assessed energy intake using 24 hours recall method which has limited usefulness in estimating individual dietary intake.[32]

5.4 : Height

Height represents a surrogate for dietary and hormonal influences prior to adulthood that might affect the risk of prostate cancer significantly. There was a moderate positive association between increasing height and risk of advanced disease (upper quartile vs. lower quartile: RR. 1.62; 95% CI. 0.97-2.73).[33] Height was also associated strongly with prostate cancer risk in men who have a positive family history of the disease. Studies have also shown that tallness had a strong direct association with metastatic disease [RR 2.29; 95% CI 1.04-5.05].[34]

5.5: Male Pattern Baldness

Male pattern baldness and prostate cancer share some common risk factors like aging, androgen levels and heredity. According to report of one cohort study which tried to find out the correlation between male pattern baldness and risk of prostate cancer, men with male pattern baldness have 50% higher risk (RR. 1.50; 95% CI.1.12-2.01).[35]

5.6: Sexually Transmitted Infections

There is an inconsistent observation that infection with Human Papilloma Virus and syphilis is related to higher risk of prostate cancer. One study suggested that men with STDs had 2-3 fold higher risk, especially with Gonorrhea.[36]

5.7 Frequency of Sexual Activity

Increased sexual frequency, particularly ejaculatory frequency, may be associated with increased risk (RR.1.2 95% CI. 1.1-1.3); but other studies have not identified any association.[37] Since researchers used the case-control designs which collected data from the past and considering the nature of the questions, there was a chance of recall bias in these studies. Recent prospective study reported that ejaculatory

5.8: Vasectomy

There is an inconsistent observation that individuals with vasectomy have higher risk as compared to the control population. However, several other studies have shown modest positive association. There might be an issue of detection bias in these studies since men undergoing vasectomies are more likely to have prostate cancer detected than the men who do not.[39]

5.9: Sedentary Life-Style

Observations have demonstrated that men with long term physical activity have lower risk as compared to those with sedentary lifestyle. Physical activity may decrease levels of free and total testosterone, reduce obesity and enhance immune system, all of which may contribute in protecting these men from prostate cancer.[40] However, due to variations in classifying physical activity in different epidemiological studies, many reported inconsistent results in this regard.

5.10: Medical conditions and use of medicines

Diabetic patients may have lower risk. However, this effect was observed only among whites and Hispanics, whereas the protection in blacks was not marked.[41] Exact mechanism is still unclear, but higher levels of testosterone in blacks might explain the lack of this protective effect. Furthermore, patients with liver cirrhosis also have lower risk of prostate cancer.[42] It has been postulated that chronic inflammatory states may either initiate or promote cell proliferation in prostate gland. Moreover, it has been observed that higher intake of anti-inflammatory drugs, NSAIDs and aspirin, is associated with reduced risk. Further evidence came from a meta-analysis of 12 studies, which indicated that use of aspirin was associated with 15% reduction in prostate cancer risk.[43]

5.11: Tobacco Smoking & Alcohol Consumption

There is an inconsistent observation that smokers have higher risk of prostate cancer. It was found that in men who smoked 20 cigarettes per day, risk of prostate cancer was increased nearly 3 folds as compared to those men who were nonsmokers. Moreover, smokers had 20-30% increased mortality risk.[44] In contrast, alcohol consumption had no significant association with prostate cancer risk. This might be attributed to the effect of alcohol on metabolic clearance of testosterone, but few studies have suggested that heavy alcohol consumption(22-56 drinks per week) can increase the risk (OR, 1.4, 95% CI, 1.0-1.8) of prostate cancer.[45]

5.12: Socioeconomic Factors

Social factors such as income and education do not directly relate to the risk, but are surrogate measures for other factors like diet, access to medical care and awareness about the disease. Social factors do influence the mortality pattern in society. Differences in socioeconomic status do not apparently account for marked differences in prostate cancer risk.[46] On the other hand; socioeconomic factors may influence the likelihood of prostate cancer diagnosis.

Conclusion

Etiology of prostate cancer is still obscure. International variation in cancer incidence among different populations suggests that more environmental factors should be searched as potential risk factors for the disease. These risk factors may range from chemical and occupational exposures to change in lifestyle and dietary pattern. Lifestyle has emerged as a major modifiable determinant of health and disease during the last two-three decades. Identification of these modifiable risk factors not only will guide public health policy for cancer control in community, but also help to make preventive strategies in order to reduce the burden of prostate cancer in population.

Acknowledgments

We are grateful to librarian of Institute of Public health Lahore for allowing the access to journals and textbooks for the review. We also like to extend our gratitude to the staff of Baillieu Library, University of Melbourne for online access to journals and reading material.

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