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EDITORIAL

Gene-Environmental Interaction and Prostate Cancer: The Indian Scenario

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Prostate cancer remains one of the most prevalent and least understood of all human cancers. It has now become the fifth most common cancer, and second most common cause of cancer related death amongst men around the world. Prostate cancer rate may vary widely as it is influenced by genetics, culture, diet and/or environmental factors. Gene-environmental interactions have a particularly deep impact [1].

Prostate cancer incidence and mortality rate are different in diverse geographic regions and racial ethnic population. Its incidence is highest amongst developed countries compared to the developing world. The incidences in India are less than one tenth of the cases seen in the United States of America and one fifth of the rate seen in United Kingdom [2]. However, a consistent increase in incidence of prostate cancer has been observed in Asian countries over the last two and half decades, presumably due to shifts in diet and other life style factors [3]. A sharp increase in the incidence of prostate cancer has been reported in five major cities of India namely Mumbai, Chennai, Bangalore, Delhi and Bhopal over a period of last two decades. Moreover, there has been statistically significant increase in the incidence of prostate cancer in all cities [4]. In Delhi, prostate cancer has now become the fifth most common cancer. The incidence is higher amongst North Indians as compared to South Indians and it is rapidly increasing [2]. Due to increase in life expectancy, the proportion of elderly men in India is projected to rise to 15% in the year 2050 from 5% in 2003, leading to tremendous increase in the incidence of prostate cancer cases [5].

Several genes have been identified to have a role in the susceptibility to cancer. Evidence indicates that interaction between various inherited cancer susceptibility genes (also known as risk-modifier genes), particularly genes whose polymorphic variants are responsible for impaired ability to metabolize harmful compounds like environmental carcinogens; steroidal hormones etc could affect an individual's cancer susceptibility. Individual susceptibility to cancer from environmental agents and steroidal hormones may be influenced by polymorphism in such metabolic susceptibility gene families. Most of these genes like those of Cytochrome P450 (CYP) and Glutahtione S-transferase (GST) families are associated with low risk but

may have a large population impact because the relevant polymorphisms might be highly prevalent. For example, a polymorphism which increases cancer risk only by 50% but is also present in half of the population would account for 20% of all cases, similar to a high-risk gene with an increased risk of 5-fold which is present in only 5% of the population [6]. The Indian population is a major distinct ethnic group representing one-sixth of the total world population [7]. However, only a few studies have analyzed the polymorphic distribution of drug metabolizing enzyme genes among Indians, especially North Indian and hence is an important area of research [8-10]. Use of environmental chemicals has increased exponentially in recent times and pesticides are the largest class of these chemicals which get intentionally or unintentionally released into the environment. Use of pesticides is a boon for humans for its tremendous role in agriculture and public health. However, inappropriate use of pesticides has led to adverse effects on human health [11]. India is one of the leading pesticide consumers in the world. However, in India, poor safety measures during application and handling of these carcinogenic compounds has led to widespread dispersion of these harmful and carcinogenic compounds, which can be harmful for humans [12].

Majority of the pesticides identified till date are classified by WHO as being either 'extremely', 'highly' or 'moderately' hazardous to humans. Stockholm Convention on Persistent Organic Pollutants (POPs) identified that ten of the twelve most dangerous POPs are pesticides [11]. Majority of India's population is engaged in agriculture and related industries and are therefore potentially exposed (occupationally and/or environmentally) to some types of pesticides either directly or indirectly [13]. Recently one of our studies found higher levels of DNA damage in workers occupationally exposed to these pesticides, a known risk factor for cancer [14]. Some of these pesticides, mainly organochlorine pesticides (OCPs) have been reported to possess estrogenic properties and are called 'xenoestrogenic pesticides'. OCPs, such as 1,1,1-trichloro-2,2-bis (p-chlorophenyl) ethane (DDT), hexachlorocyclohexane (HCH), dieldrin and endosulfan are among the most commonly used xenoestrogenic OCPs in India. Since prostate cancer is an estrogen dependent cancer it is reasonable that these pesticides may increase the risk of prostate cancer. Studies have reported that the incidence of hormone related organ cancers has increased among farmers and this is being attributed to the potential exposure to endocrine disrupting pesticides, particularly DDT and phenoxy herbicides [15].

Various genes of *CYP* and *GST* families are involved in the metabolism of many carcinogens including pesticides [16]. In India polymorphism in these genes and levels of these POPs are reported to be associated with the prostate cancer susceptibility [17]. Moreover, in recent studies from our laboratory few markers of oxidative stress were found to be significantly elevated amongst prostate cancer patients and subjects suffering from other disorders, suggesting that the mutant genotypes of GSTs may modify stress levels leading to higher risk of these disorders [18-20]. Moreover, some high risk genotypes are reported to be associated with higher DNA damage, an important risk factor of cancer [21].

Rapid increase in knowledge about the human genome and its variations in different ethnic human populations gave rise to great opportunities to incorporate genetic assessments into epidemiologic studies of multi-factorial human disorders. In particular, the study of gene-environment interactions provides a potentially powerful approach for identifying the causes of many diseases including prostate cancer. Moreover, further studies on gene-environment interactions will be helpful in 'early risk prediction, and 'personalized prevention' in the forth-coming times.

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