PREFACE

Prostate cancer is the most commonly diagnosed non-skin malignancy and the second leading cause of death as a result of cancer in most countries. There is a large variation in the prostate cancer incidence rates between racial/ethnic groups, highest among Africa, intermediate among Caucasians and lowest among Asians. Despite the substantial public health impact of prostate cancer, little is understood about its etiology. Steroid hormones, particularly androgens and to some extent estrogen appear to play a major role in the development of prostate cancer, but their precise role is not clear.

Testosterone, the major male androgen in the circulation is converted into the more potent androgen, dihydrotestosterone (DHT), which is required for the normal growth and development of prostate gland. Both testosterone and DHT have been shown to induce prostate adenocarcinomas in experimental rat models. Because normal growth and function of prostatic tissue is under the control of DHT, there has been much interest in the role of sex steroid hormones in the etiology of prostate cancer. However, despite strong biological support, there has been no consistent epidemiological link has been established between steroid hormones and prostate cancer risk.

The search for genetic markers of disease susceptibility often focuses on a gene, based on the properties and metabolic pathways of its protein product. Thus, genes involved in androgen biosynthesis and metabolism cascade have been identified as possible modifiers for prostate cancer. Recent studies have found an association between prostate cancer risk and polymorphisms in several genes along the sex steroid pathway, including *SRD5A2*, which catalyses the conversion of testosterone to DHT. Thus, it is possible that the discrepancies among epidemiological studies investigating the link between prostate cancer and steroid hormones may be due in part to polymorphisms in genes involved in the metabolism and action of steroid hormones. Moreover, racial differences in genetic polymorphisms that have a
role in the metabolism of testosterone and other androgens may partly account for racial differences in prostate cancer risk.

Despite the availability of certain evidences, linking androgens and prostate cancer conflicting results have been yield by molecular epidemiological studies. Postulated genetic associations for prostate cancer need to be carefully validated across several studies, since early and small genetic association studies may come up with spurious findings. Moreover, no report on the Indian population is available. Some work has been carried out in our laboratory on the polymorphism of some of these genes but much remains to be done yet particularly with respect to polymorphisms in prostate cancer related metabolic genes. Work need to be carried out on some prostate cancer candidate genes also. Such work is of importance because the prevalence of prostate cancer in the population probably results from complex interactions among many genetic and environmental factors. It is possible that a set of genetic polymorphisms rather than a single polymorphism can alter hormone levels and prostate cancer risk. The development of polymeric model for prostate cancer incorporating multiple loci from the individual genes may yield better preventive, diagnostic, and therapeutic strategies. The goal of this study was to investigate the association of prostate cancer and polymorphisms in the AR, ER, PR, CYP19, CYP17, SRD5A2 and VDR genes. Moreover there is an increasing evidence of cross talk between estrogens and androgens in regulating gene expression in the prostate. The circulating estrogens can compete with androgens for binding to sex hormone-binding globulin, and it is generally assumed that sex hormone-binding globulin synthesis is regulated by and is a reflection of the estrogen/androgen balance. To the best of our knowledge, there have been no previous studies on the relationship of polymorphism with prostate cancer risk, nor have there been any studies on the interactions among these polymorphisms on prostate cancer risk in Indian patients. Therefore, we have looked into the polymorphic forms of hormone receptor genes in Indian prostate cancer patients. It is possible that individual and combined genetic variations in these genes, which may alter the availability of sex steroid hormones, can alter an individual's
risk of prostate cancer. It is with this idea in mind the present project was undertaken.

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