1. Introduction

Cancer is a generic term that refers to a group of chronic diseases characterized by the uncontrolled growth of abnormal cells within the body. Normally, cells divide and replicate to replace worn-out ones or to repair some form of injury to tissues of the body. Normal cells wear out and die, after a predictable period only. Cancer cells do not grow, divide and die in the same predictable fashion as the normal cells. Rather they grow, divide and create more abnormal cells, which outlive normal cells. These abnormal cells often spread to other body parts, invading other organs or systems (Metastasis). Recently it has been reported that in the past 30 years the global burden of cancer, based on the incidence of new cancer cases and annual deaths, has doubled. The burden of cancer, however, is not equally distributed, and this represents a major concern. Today 63% of cancer cases occur in developing countries. It has been estimated that across the globe there will be 12.9 million new cases diagnosed this year, and the worldwide toll is predicted to rise to 27 million new cancer cases and 17 million deaths by the year 2030 (NCI bulletin, 2009).

It has become the leading cause of deaths in the last 50 years, breast cancer being the most common malignancy in women and the second most common cause of cancer related mortality. On the other hand, prostate cancer is the most common solid organ malignancy diagnosed in men in Europe and the US and the second most frequent cause of cancer related deaths in men (NCI bulletin, 2009).

There are more than 100 types of cancers. They are classified according to the types of cells in which they develop. Most cancers, but not all, affect solid tissues and organs in the body. During the 1970s, scientists discovered two families of genes that play major roles in the genesis and spread of cancer:

- Oncogenes which are mutated forms of genes that cause normal cells to proliferate out of control and convert into cancer cells
- Tumour suppressor genes are normal genes that regulate cell division, repair mistakes in DNA and control apoptosis. When tumour suppressor genes malfunction, cells can grow out of control, leading to cancer.

Diagnostic methods of disease progression are essential elements for successful disease management of cancer. The early stages of cancer development
have the maximum potential for therapeutic interventions. However, these stages are often asymptomatic, leading to delayed diagnosis at the very advanced stages when effective treatments are not available. Because of the unique association of genomic changes in cancer cells with disease progression, the application of biomarkers to cancer is leading the way. They have the potential to not only identify who will develop cancer, but also to predict as to when the event is most likely to occur. In recent years, there has been an enormous effort to develop specific and sensitive biomarkers for precise and accurate screening, diagnosis, prognosis and monitoring of high risk cancer to assist with therapeutic decisions.

Prostate cancer is one of the most prevalent and least understood of all malignancies in man. Initially prostatic tumours are androgen dependant, resulting in the death of the patient. Since late 1940, there is a dramatic increase in the identification of prostatic cancer cases. The reasons are many, like increased elderly population, cancer registration and improved methods of prognosis of the disease, use of new diagnostic technologies including transrectal ultrasound guided needle biopsy, computer tomography, greater frequency of operations for benign disease and serum testing of prostate specific antigen (PSA) (Jemal et al., 2004).

The prevalence of histological prostate cancer is remarkably similar in the whole world, but clinical incidence widely varies. It indicates that although initiation rate of prostate cancer is same, but that of progression of clinically evident disease varies. This suggests that prostate cancer is an interplay of genetic and epigenetic events and both of which may be affected by environmental risk factors that act as promoters or activators. It is a multistep process involving three stages i.e., initiation, promotion and progression, mediated through various cellular, biochemical and molecular changes. It involves activation of oncogenes, loss of function of tumour suppressor gene, modulations in genes related to growth regulation, cell cycle, apoptosis, metastases and angiogenesis as well as alteration of modifier genes (metabolic, hormonal, DNA repair genes, methylation and genomic stability). Epigenetics refers to altered levels of a gene’s transcriptional activity without directly affecting its primary DNA nucleotide sequence.

Individuals with defects in mutation repair pathways are often susceptible to spontaneous or induced cancer. The molecular machinery of the repair pathways has
slowly been unraveled over the past few decades. Understanding these molecular pathways improves the prognosis of the disease and may help in finding genes involved in initiation and progression.

A malignant tumour results after a series of DNA alterations in a single cell, or clones of that cell, which lead to loss of normal function, aberrant or uncontrolled cell growth and often metastases. Several of the genes, which are frequently lost or mutated, have been identified including those whose function is to induce cell proliferation under specific circumstances (e.g., ras and myc proto-oncogenes) and genes which are programmed to halt proliferation in damaged cells (e.g., p53 and APC tumour suppressor genes). In addition, mutations in genes involved in DNA repair, cell-cycle control, angiogenesis and telomerase production also play an important role in cancer genesis. With the exception of rare familial cancers which are primarily caused by a germline inheritance of a specific mutation, a sporadic cancer may acquire mutations as a result of genotoxic exposure to external or internal agents (such as tobacco, chemicals, dietary factors, pollutants and sex hormones) resulting in DNA aberrations. The likelihood of a mutation(s) occurring and persisting in subsequent clones may be heavily dependent on the efficiency with which potentially toxic exposures are metabolized and excreted, and also the efficiency with which small mistakes in DNA replication are rectified. This progress of carcinogenesis is likely to vary strongly between individuals because of the population variability in polymorphic genes that regulate these processes. Changes in the patterns of methylation have been associated with the altered expression of a number of genes involved in cell cycle control and apoptosis, including p16, GSTP1, INK4a, RASSFIA, RAR-β, FHIT, APC, MGMT, H- and E-cadherins among many others in various carcinomas (Esteller et al., 2001). Silencing of tumour suppressor and tumour-related genes by hypermethylation at promoter CpG islands is one of the major events in human tumourigenesis.

The present study is an effort to analyze, polymorphisms in XPC and XPD repair genes, GSTP1 exon 5 and exon 6 metabolic genes and their association with the etiology of prostate cancer and correlation of the same. The methylation pattern of GSTP1 and MGMT gene has also been studied in prostate cancer, BPH patients and healthy controls to correlate it with the incidence and progression of this cancer.