INTRODUCTION

According to World Health Organization report, during 2005 cancer killed approximately 826,000 people in India, of which, nearly 519,000 were under the age of 70 years (WHO, 2005). Its incidence, like most other malignancies, increases with age, though it can occur at any age (Lynch and Cohen, 1995). Several important risk factors have been identified for bladder cancer; these include cigarette smoking, exposure to chemicals such as aniline dyes, benzidine compounds, aromatic amines; "slow acetylators" metabolic phenotypes and the presence of chronic inflammation or infection of the bladder. Histologically, greater than 90% of bladder cancers are transitional cell carcinomas, squamous cell cancers and adenomacarcinomas constituting 5 to 6% and 1% respectively (Konety et al., 2000).

Around 70% of all transitional cell carcinomas are classified as superficial lesions i.e., they do not invade more extensively than into the lamina propria. They comprise of a heterogenous group ranging in both histologic grade (low or high) and stage (Ta confined to the mucosa, T1 invasive into the lamina propria, CIS carcinoma in situ) (Bostwick et al., 1999). Even with early adequate treatment, there is an overwhelming propensity of bladder carcinoma to recur. Upto 70% of superficial tumours recur within 5 years, a figure that rises to 90% in 15 years. Over 20% of the superficial tumours progress to invasive disease with a poor prognosis (Carpinito et al., 1996; Sanchez-Carbayo et al., 1999). This entails an intensive follow up programme to detect recurrences at the earliest. Presently cystoscopy remains the primary diagnostic modality to detect bladder carcinoma.

Cystoscopy has a reported sensitivity of over 90% to detect
tumour (Sharma et al., 1999). It, however, is invasive, uncomfortable and expensive, apart from the loss of man hours at work and the requirement for a trained urologist. Moreover, the classic recommendation for cystoscopic surveillance in bladder cancer has been, once every 3 months for first year, every 6 months for the second year, and yearly thereafter. These are authority based opinions with little empirical backing. Such schedules may be inadequate for high risk patients and overzealous for individuals with solitary, low grade, low stage lesions (Messing et al., 2002). It is also limited by low specificity and positive predictive value when used to evaluate microscopic haematuria or chronic irritative voiding symptoms (Sharma et al., 1999).

To detect carcinoma of urinary bladder noninvasively at initial presentation, or at follow up, cytological assessment remains the standard assay (Saad et al., 2001). It is, however, plagued by low sensitivity, on an average less than 50% and as low as 30% in low grade, low stage disease (Sharma et al., 1999). It is laboratory based investigation, cumbersome and expensive, requiring trained personnel for its interpretation, with slow sample collection and minimal potential for automation. Bladder cancer is a chronic illness with no definite and suitable curative measures. The main goal in their management is to diagnose the primary and recurrent tumour as early as possible, while it is amenable to local resection.

There is thus a need for simpler detect urothelial malignancies. The challenge has been and remains, to develop regimes acceptable for monitoring of asymptomatic patients, for follow up and detection of primary and recurrent of bladder cancer.

It has been established that cancer can be promoted and/or exacerbated by cytokines.

Cytokines secreted by tumour and inflammatory/immune cells can either promote tumour development and tumour cell survival or exert antitumour effects. Chronic inflammation develops through the
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action of various inflammatory mediators, including TNF-α, IL-6, leading to eradication of antitumour immunity and accelerated tumour progression. However, IL-10, through antiinflammatory effects, and IL-12, through activation of CTLs and NK cells and expression of cytotoxic mediators, can lead to tumour suppression (Lin and Karin, 2007). In addition, tumour suppressor genes such as \(P14\) and \(P16\) with specific effect on cell cycle have impact on cell proliferation and development of cancer. It is possible that genetic and epigenetic changes in these genes may lead to development of cancer.

Our understanding of cancer cell biology should lead to better ways of diagnosing and treating the diseases. Anticancer therapies can be designed to destroy cancer cells preferentially by exploiting the properties that distinguish them from normal cells, including the defects in their DNA repair mechanisms, cell cycle checkpoints and apoptotic pathways. As we are able to determine which genes are amplified, or are deleted or mutated in the cells of any cancers, we would be able to more accurately tailor treatment for the individual patients. By understanding the normal control mechanisms and exactly how they are subverted in specific cancers, it becomes possible to device drugs to target cancers more precisely (Alexander et al., 2001).

Single nucleotide polymorphism (SNP) research can be used as genetic marker in order to disease susceptibility at individual and population levels, prognosis of cancer, and gene therapy and drug resistance in chemotherapy.

Bladder cancer is the second commonest cancer in India and its incidence seems to be increasing (Tongaonkar et al., 1995). According to World Health Organization (2005) amongst the 10 leading causes of cancer deaths in India, bladder cancer ranked 8th and the subsequent death rate per 100,000 people was 4. Various attempts have been made to predict the occurrence and factors involved in the causation of a disease, as it's essential for decision making in public health issues related to it.
Very few studies have examined the relationship and correlation between genetic polymorphism, main etiological factors and uro-epithelial cancer, especially in developing countries and the data with respect of Indian population (also recognized as one of genetic diversity region in the world) have not been worked out or documented yet. It is because of this the present project was undertaken.