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Editorial Commentary

Genitourinary malignancies in India: Laying the foundations for the future

Genitourinary (GU) cancers form less than one-fifth of all cancers reported in India. Except prostate cancer, the age-adjusted incidence rate (AAR) for GU cancers is <5.[1] Most of the data reviewed report the incidence of these cancers from hospital-based registries. Although these data give a glimpse of the occurrence of these cancers, there is dearth of any prospective datum and paucity with respect to treatment patterns and outcomes.

The steep increase in the incidence of prostate cancer in the last two decades is striking.[2] Although the incidence continues to be less than one-tenth of Western countries, there has been a doubling of incidence in the Delhi and Bengaluru cancer registries. It is ranked second in the Delhi and Thiruvananthapuram registries. The highest incidence is in Kamrup urban registry with an AAR of 11.2. This rate of increase is faster than that of other "lifestyle cancers" such as breast, colon, and uterus (which has doubled over the past three decades in the Bengaluru and Chennai registries).

Reasons for disproportionate rise in prostate cancer compared to rest of the GU sites are unclear. Although factors such as obesity, hypertension, and smoking have been associated with prostate cancer,[3] we are yet to pin down the reason for this increase. As more men get tested for prostate-specific antigen as part of their regular annual health check, the incidence is bound to increase. It would be interesting to see if there has been a disproportionate increase in early stage cancer as compared to the advanced stages.

As in rest of the world, there is a male preponderance in renal and urinary bladder cancers. However, the male to female ratio is significantly higher than Western series.[4] Evidence regarding the associations of age at menarche, parity, age at first birth, and exogenous hormone use with bladder cancer risk is conflicting with the larger studies showing a lack of association.[5] There is preclinical evidence that activation of estrogen receptor-beta that is a tumor suppressor gene by estrogen may decrease the incidence of renal cell carcinoma.[6] It is more likely that this disproportionate difference in India is more likely to be a result of socio-economic issues.

The other observation that most of these studies make is the earlier onset of disease. The actual reason for this early onset remains debatable. It is a fact that we have a larger population of these younger men and women with GU cancers. Most of these, notably, prostate cancers are aggressive in the young and are associated with specific molecular changes. These include more frequent activation of the androgen-androgen receptor axis as reflected by the TMPRSS2-ERG gene activation, mutations in the fatty acid synthase gene, and increased activation of inflammatory cytokines. In contrast, the presence of HOXB13 mutation is associated with a more favorable prognosis even in young.[7] Looking for genetic predisposition such as mutated BRCA1 genes in these young patients may be relevant.[8] This also gives us the unique opportunity to do clinical trials targeting specific molecular changes in these diseases getting us a step closer to personalized medicine. The more recent trials of early institution of chemotherapy in advanced prostate cancer, especially those with aggressive high volume disease, may be more applicable to our young population with this disease.

Similarly, there seems to be a higher incidence of nonclear cell renal cell carcinoma compared to Western series.[9] All advances in targeted therapy have been made in clear cell carcinoma. Nonclear cell type is associated with poorer outcomes and a difference set of molecular abnormalities. There is a need to generate more data on nonclear cell renal cell carcinoma in terms of both epidemiology and treatment.

Penile cancer is rare in the West. In the series reported by Pahwa *et al*., a significant number of penile cancers are advanced at diagnosis.[10] Penile cancer is associated with human papillomavirus (HPV) 16 DNA integration in 20–30% of all cases.[11,12] There may be a role in the future for the potential benefit of current and new HPV vaccines in the reduction of HPV-related penile cancer.

We all understand the paucity of data not only in GU malignancies but also in all cancers in India. These data certainly lay the foundation for what research this country needs and should focus on better and more efficient collection and analysis of epidemiological data, and designing of clinical trials that are relevant to this country is the need of the hour, and I do not see any reason why that cannot be done.

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