Clinicopathological profile of malignancies treated in a urology unit over a period of five years

K. Sutharshan[1], B. Balagobi[1], S. Gajasinghe[1], S. Sasikumar[1], A. Weligamage[1], M. Ishak[1], H. Maddumage[2], A.M. Abeygunasekera[1]

1 Department of Urology, Colombo South Teaching Hospital, Dehiwala, Sri Lanka

2 Department of Pathology, Colombo South Teaching Hospital, Dehiwala, Sri Lanka

Key words: Urological carcinoma; Sri Lanka; asia; prostate; bladder; kidney

Abstract

Objective

To identify the clinico-pathological profile of urological malignancies treated in the urology unit of a tertiary care hospital in Sri Lanka.

Materials and methods

Data related to all newly diagnosed and histologically confirmed malignancies in a urology unit of a tertiary care hospital in Sri Lanka were recorded prospectively over a period of five years from 1st of January 2011 to 31st of December 2015.

Results

There were 386 prostate cancers, 193 bladder tumours, 173 renal tumours, 13 upper urinary tract carcinomas, eight penile cancers, seven testicular malignancies, one urethral carcinoma and two urachal carcinomas during the study period. Gleason score of 8 or more prostate cancers were seen in 164 (42.5%) patients. Metastases were present in 59.8% of patients with prostate cancer. Muscle invasive urothelial cancers constituted 31.4% patients with bladder carcinoma. Primary carcinoma-in-situ of the bladder was seen in only one patient. Average age at diagnosis of renal cell carcinoma was 56.9 years with a male to female ratio of 3.5:1.

Conclusion

Renal cancers in Sri Lanka occur at an earlier age than the developed countries. They are diagnosed at an early stage similar to the developed world in contrast to the late diagnosis of prostate and bladder malignancies in Sri Lanka. Most prostate cancers are high grade with a Gleason score of 8 or more. Primary carcinoma-in-situ of bladder is extremely rare in Sri Lanka.

Correspondence: A.M. Abeygunasekera
E-mail: amabey@sltnet.lk
DOI: http://10.4038/sljs.v34i4.8313

Introduction

Total health expenditure as a share of GDP in Sri Lanka is around 3.5% [1]. Twenty six Urological surgeons serve the country's population of 20 million. With universal health care and a robust public health network across the country, Sri Lanka has made noteworthy achievements in health outcomes compared to other developing countries [2]. With the changes in the socioeconomic parameters of the Sri Lankan society non communicable diseases have become the major health challenge of the new millennium. Malignancies make a significant portion of the non-communicable diseases worldwide as well as in Sri Lanka [3].

Different countries have populations of varying ethnicities with potentially different genetic makeup. In addition to genetic differences, the pattern of cancers differs according to different socio-cultural factors inherent to the index population. In the absence of a comprehensive national cancer registry, data maintained at individual units or at institutional level are useful to identify epidemiological and demographic patterns. Our aim of the study was to identify the clinico-pathological profile of urological malignancies treated in the urology unit of a tertiary care hospital in Sri Lanka.

Materials and methods

A cancer registry was maintained prospectively at the urology init of Colombo South Teaching Hospital. Data related to all newly diagnosed malignancies were recorded prospectively. The data were updated as the patients' follow up continued in the clinic. The data belonging to patients over a period of five years from 1st January 2011 to 31st December 2015 were analysed.

Histopathologcal evaluation was done according to the World Health Organisation (WHO) and International Society of Urological Pathology (ISUP) classification 2004 [4]. All patients included in the study had their diagnosis confirmed by histopathological evaluation. Tumour staging was done using the TNM classification of the Union for International Cancer Control 2009 [5]. Approval for the study was obtained from the Ethics Review Committee of the Institute.

Organ	Number
Prostate	386
Bladder	193
Renal	173
Upper tract urothelial	13
Penile	8
Testicular	7
Urethral	1
Urachal	2
Total	783

Table 1. Distribution of tumours according the site of origin

Variable	Number (%)
Average age (years)	70.8
PSA level (ng/ml)	
<10	25 (6.5)
11-20	60 (15.5)
21-50	68 (17.6)
51-100	66 (17.1)
>100	149 (38.6)
Data not available	18 (4.7)
Mode of diagnosis	
TRUS biopsy	223 (57.8)
Trans-rectal biopsy	93 (24.1)
TURP chips	70 (18.1)
Gleason sum score	
=6	68 (17.6)
7	137 (35.5)
=8	164 (42.5)
Data not available	17 (4.4)
Stage of disease	
Localised	69 (17.9)
Locally advanced	86 (22.3)
Metastatic	231 (59.8)
Main modality of therapy	
Radical prostatectomy	5 (1.3)
Radical Radiotherapy	59 (15.3)
Androgen Deprivation Therapy	299 (77.4)
Surveillance	23 (6.0)
Total	**386 (100)**

Table 2. Characteristics of patients with prostate carcinoma

Tumour type	Number
Urothelial tumours (n=172)	
Infiltrating urothelial carcinoma	133
With squamous differentiation	14
With glandular differentiation	2
Micropapillary	1
Clear cell variant	1
Plasmacytoid	1
Non-invasive urothelial neoplasms (n=20)	
Urothelial carcinoma-in- situ	1
Non-invasive papillary urothelial carcinoma, low grade	17
Non-invasive papillary urothelial neoplasm of low malignant potential	2
Squamous neoplasms (n=14)	
Squamous cell carcinoma	14
Glandular neoplasms (n=5)	
Adenocarcinoma (Enteric type)	5
Mesenchymal tumours (n=1)	
Leiomyosarcoma	1
Haematopoietic and lymphoid tumours (n=1)	
Lymphoma (large B cell)	1
Total	193

Table 3. Histopathological types of bladder tumours

Stage		Number
pT_a	***(n=19)***	
	Low grade	17
	High grade	2
pT_1	***(n=94)***	
	Low grade	62
	High grade	32
$\geq pT_2$	***(n=54)***	
	Low grade	6
	High grade	48
Uncertain		5
Total		172

Table 4. Pathological stage and grade of urothelial carcinomas of bladder

Results

Table 1 shows the number of malignancies in different organs of the urinary tract. Prostate cancers were the commonest (n=386) followed by bladder (n=193) and renal (n=173) tumours. There were 386 prostate cancers. The characteristics and primary modality of treatment of prostate cancers are given in table 2. The average age at diagnosis of prostate carcinoma was 70.8 years. Only 12 (3%) patients had screening detected prostate cancer. One hundred and sixty four (42.5%) patients had Gleason score 8 or more cancers. Two hundred and thirty one (59.8%) patients had evidence of metastases at the time of diagnosis. Out of the 299 patients who required androgen deprivation therapy, 282 (94.3%) patients opted to have surgical orchidectomy.

There were 193 patients with bladder tumors during the five-year period. Average age at diagnosis was 65 years with a male to female ratio of 4.2:1. Histological types of bladder tumours are given in table 3. Infiltrating urothelial carcinoma was seen in 133 patients. There was only one primary carcinoma-in-situ found among the bladder tumours. There were 14 (7.3%) patients with squamous cell carcinoma and five (2.6%) with adenocarcinoma of the bladder. In addition to the above primary malignant neoplasms in the bladder, five patients had metastatic deposits in the bladder during the five year study period. Their primary malignancies were breast carcinoma, papillary renal cell carcinoma - type II, ovarian carcinoma, carcinoma of the stomach and melanoma of the skin. One patient had an inflammatory myofibroblastic tumour of the bladder. The pathological evaluation of the bladder cancers revealed that 47.7% (82/172) were high grade and 31.4% (54/172) were muscle invasive (Table 4).

There were 173 renal tumours (Table 5) out of which, 164 were renal cell carcinomas. The male to female ratio of RCC was 3.5:1. The average age at diagnosis of renal cell carcinoma was 56.9 years. The commonest (81%) renal tumour was clear cell renal cell carcinoma (Table 5). There were 25 papillary renal cell carcinomas. Most (70%) patients had radical nephrectomy as the primary mode of treatment for renal tumours (Table 6).

Partial nephrectomy was possible in 42 (24.3%) patients. Facilities for radiofrequency ablation is available at the institute and three patients including one with von Hippel-Lindau disease were treated with radiofrequency ablation. Table 6 shows the pathological stage of the renal cell carcinomas. Pathological staging of renal cell carcinomas which underwent surgery are given in table 7. Twenty (13%) patients with renal cell carcinoma had metastases at the time of diagnosis.

Upper tract urothelial tumours were seen in 13 patients during the five year study period. All of them were urothelial carcinomas. Ten (76.9%) of them were men. Average age of patients with upper tract urothelial carcinoma was 69.7 years. Eight of them had high grade urothelial carcinoma, while five had low grade disease. Pathological stage was pT1 in six cases and pT3 in seven patients. Twelve of them underwent nephroureterectomy and one had segmental resection of the lower ureter with Boari flap reconstruction as he had a single functioning kidney.

There were eight penile cancers with an average age at diagnosis of 59.8 years. Seven had squamous cell carcinoma while one had a basaloid cell carcinoma. Five of the squamous cell carcinomas were well differentiated while two were moderately differentiated. Pathological stage was pT1 in five, pT2 in two and pT3 in one. Three patients had N1 stage disease and one patient had N2 stage lymph nodes. Mode of surgery included total penectomy in two, partial penectomy in five and glansectomy in one.

There were seven testicular malignancies. The histological types included classic seminoma in three, mixed germ cell tumour in two, choriocarcinoma in one and non-Hodgkins lymphoma in one. When the patient with lymphoma was excluded (who was 79 years old) the average age of patients with testicular malignancies was 31.5 years. The pathological stage was pT1 in five and pT2 in one. One of them had N3 disease while one had lung metastases.

The patient with primary urethral carcinoma had total penectomy and the histology was a squamous cell carcinoma. One male (age 51 years) and one female (age 47 years) patient had urachal carcinomas. Both had partial cystectomy with excision of urachal ligament and umbilicus and pelvic lymphadenectomy.

The histology revealed mucinous type and enteric type of adenocarcinoma in the two patients respectively.

	Number (%)
Renal cell tumours	
Oncocytoma	5 (2.9)
Clear cell renal cell carcinoma	132 (76.3)
Multilocular clear cell renal cell carcinoma	2 (1.1)
Papillary renal cell carcinoma type 1	8 (4.6)
Papillary renal cell carcinoma type 2	17 (9.8)
Chromophobe renal cell carcinoma	3 (1.7)
Xp11 translocation renal cell carcinoma	1 (0.5)
Renal cell carcinoma unclassified	1 (0.5)
Nephroblastic tumours	
Nephroblastoma (adult Wilms tumour)	2 (1.1)
Mesenchymal tumours	
Angiomyolipoma (atypical)	1 (0.5)
Solitary fibrous tumour	1 (0.5)
Total	173 (100)

Table 5. Histopathological types of renal tumours

Treatment	Number (%)
Radical nephrectomy	121 (69.9)
Partial nephrectomy	42 (24.4)
Radiofrequency ablation	3 (1.7)
Tyrosinekinase inhibitors only	3 (1.7)
Palliative care only	4 (2.3)
Total	173 (100)

Table 6. Primary treatment modality of all renal tumours

Pathological stage	Number (%)
T_{1a}	44 (28.6)
T_{1b}	35 (22.7)
T_2	36 (23.4)
T_3	36 (23.4)
T_4	3 (1.9)
N_0	148 (96.1)
N_1	1 (0.6)
N_2	5 (3.3)
Metastatic	20 (13.0)

Table 7. Pathological stage of renal cell carcinomas after surgery (n = 154)

Discussion

The latest data available from National Cancer Registry of Sri Lanka is for year 2007. According to that, there have been 391 cases of prostate, 151 cases of bladder and 106 cases of renal cancers for the whole country in 2007 [3]. The total number of prostate, bladder and renal cancers in our study cohort over five years exceeds the above reported figures. Hence our study results can be considered as representative enough of urological cancers of the country in most aspects.

The commonest urological cancer treated in the unit was prostate carcinoma. According to the National Cancer Registry of Sri Lanka prostate carcinoma is the 9th most common cancer in Sri Lankan men [3]. In Asia prostate carcinoma is the sixth most frequent cancer in men [6]. Most prostate cancers (59.8%) in Sri Lanka still presents at the metastatic age similar to other South Asian countries and Indonesia [6,7]. Only 3% were screening detected.

There is no screening programme for prostate cancer in Sri Lanka. A small number of patients get their serum PSA checked during annual medical checkups done by their employers. They constituted the small number of screening detected cancers in our study cohort. A large proportion (42.5%) of patients with prostate cancer had a Gleason score of 8 or more.

When compared with other Asian countries this pattern is similar to that found in China, Hong Kong and Taiwan [6]. Whether this is due to the late presentation or due to an unknown risk factor is debatable [8]. Only 17.6% were

Gleason 6 cancers. Active surveillance is done very rarely due to technical problems like poor compliance and commitment to rigorous follow up.

Surgical orchidectomy is the mostly used (94.3%) form of androgen deprivation therapy which could be considered an attractive option in developing countries with large rural communities [8]. Most patients with organ confined disease in our study preferred radical radiotherapy over radical prostatectomy.

Urothelial tumours constituted 89% of bladder malignancies. Muscle invasive tumours were seen in 31.4% indicating delayed presentations or de novo aggressive disease. Although this is higher than the proportion in the western world, is much less than the 74.1% in China [9]. A higher incidence of squamous cell carcinoma (7.3%) compared to the western world and some other Asian countries is evident in this study.

The proportion of squamous cell carcinoma in China is around 1.9% [9]. Whether this is related to environmental risk factors that operate in Sri Lanka is unclear [10]. Primary carcinoma-in-situ of the bladder is almost unheard of in Sri Lanka. This is so in other south Asian countries like India too [11,12].

However in China, carcinoma-in-situ of the bladder is seen in 2.4% of urothelial carcinomas [9]. Although the exact reason is unknown it could be due to the high prevalence of BCG vaccination in Sri Lanka. Intravesical BCG is well known to be effective in treatment of primary carcinoma in situ of the bladder. In 1929 Raymond Pearl reported a lower frequency of cancer in patients with tuberculosis [13]. He also showed that cancer survivors had a higher incidence of healed tuberculosis than those who succumbed to malignancy. In late 1950s it was shown that mice infected with BCG were better able to resist inoculation with cancer cells [14].

In 1969 Coe and Feldman observed a strong delayed hypersensitivity type reaction to BCG in guinea pig bladder [15]. These observations lead Morales to try intravesical BCG to prevent tumour recurrences of bladder cancer [16]. Hence it is reasonable to postulate that widespread BCG vaccination may be a potential reason for the rarity of primary carcinoma in situ in Asia. In Sri Lanka BCG vaccination is mandatory at birth and coverage is more than 90% of the population for most vaccines [2].

Unlike prostate and bladder cancers, renal cancers of our study have been diagnosed at a relatively early stage similar to developed nations [17]. This may be due to the widespread availability of abdominal ultrasonography facilities in the country. However the average age at diagnosis of renal cell carcinoma is much lower than in the developed countries of Asia and Europe [15,16]. In Japan it is 63.9 years and in Sweden it is 67 years [17,18]. The average age at diagnosis of renal cell carcinoma in our study is similar to that of neighbouring India [19]. Some postulate whether comparatively poor nutritional status of younger population in developing countries could be responsible for this difference [19]. The distribution of histological types of renal cell carcinoma in Sri Lanka is similar to the rest of the world [17,18].

Upper tract urothelial cancers are uncommon and accounts for 5% of urothelial malignancies [20]. In our study cohort upper urinary tract urothelial carcinoma occurred at a ratio of 1:10.2, when compared with urothelial carcinomas of the bladder which is similar to worldwide data.

Most of the upper tract urothelial cancers of Sri Lanka are of high grade (61.6%) and are diagnosed at an advanced stage (54% were pT3 stage). However the percentages are similar to those of developed countries in Asia. In Japan 60% of UTUCs are high grade and 49% are pT3 stage [21]. Even the average age at diagnosis (69.7 in our study and 70 years in Japan) and male to female ratio (76.9% and 72% men in our study and Japan respectively) of upper urinary tract urothelial carcinoma are similar to that of our study [21]. The small number of cases of testicular and penile malignancies in this study is due to the fact that such tumours are managed by general surgeons in the country. Hence referral of such patients to urology units is minimal.

The main limitation of this study is that it is confined to a single urology unit with a specific drainage population which may not be representative of the whole population of Sri Lanka. However National cancer registry of Sri Lanka is based only on basic data collected from patients registered at oncology units of the country. Therefore robust data related to urological cancers in Sri Lanka are sparse. Furthermore publication of Cancer Registry data is delayed by many years. Hence under the circumstances, data and inferences of our study would be useful for health planners and researchers.

Conclusion

Characteristics of urological cancers appear to vary among Asian countries. Renal cancers in Sri Lanka occur at an earlier age than the developed countries. They are diagnosed at an early stage similar to the developed world in contrast to the late diagnosis of prostate and bladder malignancies in Sri Lanka. Most prostate cancers are high grade with a Gleason score of 8 or more. Primary carcinoma-in-situ of bladder is extremely rare in Sri Lanka.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

References

1. Sri Lanka state of the economy 2015, Institute of Policy Studies of Sri Lanka, 2015
2. World Health Statistics 2014, World Health Organization
3. Cancer Incidence Data: Sri Lanka year 2007. National Cancer Control Programme, 2013
4. Eble JN, Sauter G, Epstin JI, Sesterhann IA. World Health Organization Classification of Tumours. Pathology and genetics of Tumours of the Urinary System and Male genital Organs, IARC Press: Lyon. 2004: p 90
5. Sobin LH, Gospodariwicz M, Wittekind C Eds TNM Classification of Malignant Tumours, Wiley-Blackwell, New York, USA. 7th edition, 2009
6. Chen Rui, Shancheng Ren, Yiu Ming Kwong, Fai Ng Chi, Cheng Wai Sam, Ian Lap Hong, et al. Prostate cancer in Asia: a collaborative report. *Asian J Urol* 2014; 1: 15-27 https://doi.org/10.1016/j.ajur.2014.08.007
7. Zeigler-Johnson Charnita M, Rennert H, Mittal R Devi, Jalloh Mohamed, Sachdeva Rajeev, Malkowicz S Bruce, et al. Evaluation of prostate cancer characteristics in four populations worldwide. *Can J Urol* 2008; 15; 4056-64
8. Abeygunasekera Anuruddha M, Wijayarathna Suranga N, de Silva Kusal, Gobi Upayasekeram, Suvendran Swarna, Weerasinghe Sujeeva. Clinicopathological characteristics and primary treatment of prostate cancer in a urology unit of Sri Lanka. *J Can Res Ther* 2015; 11: 780-5 https://doi.org/10.4103/0973-1482.140839
9. Li Kaiven, Lin Tianxin, Xue Wei, Mu Xin, Xu Enci, Yang Xu, et al. Current status and treatment of bladder cancer in China – analysis of Chinese bladder cancer consortium database. *Asian J Urol* 2015; 1: 63-6
10. Sasikumar S, Wijayarathna KSN, Karunaratne KAMS, Gobi U, Pathmeswaran A, Abeygunasekera Anuruddha M. Pathological characteristics of primary bladder carcinoma treated at a tertiary care hospital and changing demographics of bladder cancer in Sri Lanka. *Adv Urol* 2015;2015:5751647
11. Singh Laishram Rajsh, Paokai Kipgn, Sharmila Laishram, Sucheta Khuraijam, Chandra Sharma Durlav. Urothelial tumours of the urinary bladder in Manipur: A histopathological perspective. *Asian Pacific J Cancer Prev* 2012; 13: 2477-9 https://doi.org/10.7314/APJCP.2012.13.6.2477
12. Biswas Ranu Roy, Mangal Sristidhar, Guha Debasish, Basu Keya, Karmakar Dilip. An epidemiological study of cases of urothelial carcinoma of urinary bladder in a tertiary care centre. *J Krishna Institute Med Sci Uni* 2013; 2: 82-8.
13. Pearl R. Cancer and tuberculosis. *Am J Hygiene* 1929; 9: 97-101
14. Old LJ, Clarke DA, Benacerraf . Effect of bacillus cCalmette-Guerin infection on transplanted tumours in the mouse. *Nature* 1959; 184-291
15. Coe JE, Fledman JD. Extracutaneous delayed hypersensitivity, particularly in the guinea-pig bladder. *Immunology* 1966; 10: 27-30
16. Morales A, Eidinger D, Brice AW. Intravesical bacillus Calmette -Guerin immunotherapy of superficial bladder cancer. *J Urol* 1980; 124: 38-40
17. Thorstenson Andreas, Harmenberg Ulrika, Lindblad Per, Holmström Benny, Lundstam Sven, Ljungberg Börje. Cancer characteristics and current treatments of patients with renal cell carcinoma in Sweden. *BioMed Res Int* 2015; 2015: 456040
18. Kanayama Hiro-omi, Fukumori Tomohary, Fujimoto Hiroyuki, Nakanishi Hiroyuki, Ohyama Chikara, Suzuki Kazuhiro, et al. Clinicopathological characteristics and oncological outcomes in patients with renal cell carcinoma registered in 2007: The first large-scale multicenter study from the Cancer Registration Committee of the Japanese Urological Association. *Int J Urol* 2015; 22: S1-S7 https://doi.org/10.1111/iju.12826
19. Agnihotri Shalini, Kumar Jatinder, Jain Manoj, Kapoor Rakesh, Mandhani Anil. Renal cell carcinoma in India demonstrates early age of onset and a late age presentation. *Indian J Med Res* 2014; 140: 624-9
20. Kamihira O, Hattori R, Yamaguchi A,Kawa G, Ogawa O, Habuchi T. Laparoscopic radical nephroureterctomy: a multicentre analysis in Japan. *Eur Urol* 2009; 55: 1397-407 https://doi.org/10.1016/j.eururo.2009.03.003
21. Shirotake S, Kikuchi E, Tanaka N, Matsumoto K, Miyazaki H, Kobayashi H, et al. Impact of adjuvant chemotherapeutic regimen on clinical outcome in high risk patients with upper tract urothelial carcinoma: Japanese multi-institution experience. *J Urol* 2015; 193: 1122-8 https://doi.org/10.1016/j.juro.2014.10.022