ORIGINAL ARTICLE

A STUDY OF RENAL TUMOURS IN TERTIARY CARE HOSPITALS

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ABSTRACT

Introduction: Renal cell carcinomas (RCC) comprise 90% of all renal tumours and are presage of poor outcome. Very little data has been published in Pakistan regarding the clinical and pathological manifestations of the disease.

Materials and Methods: A total of 50 cases presenting with different subtypes of RCC were selected from Allied Hospital Faisalabad and Sheikh Zayed Hospital, Lahore. Clinical details were obtained from the hospital records. The fresh nephrectomy specimens were further processed according to College of American Pathologists guidelines.

Results: Mean age of the study population was 50.16 ± 11.982 years. Male to female ratio was 2.57:1. Left to right ratio was 1:1. Most tumours (n = 36, 72%) were located in the upper pole. Most common symptom was heamaturia (n = 38, 76%). Mean of the greatest dimension was 10.41 ± 4.22 cm. The most common stage of presentation was stage II (n = 21, 42%) and histological subtype was clear cell carcinoma (n = 37, 74%).

Conclusion: Renal cell carcinoma, including its chromophobe variant, is a growing malignancy in Pakistan. Delay in seeking medical care on the part of patient and inadequate facilities account for the tumour growing to a larger size and more advanced stage of malignancy in our country.

INTRODUCTION

Renal cell carcinoma (RCC) comprises 90% of all kidney tumours and is the most lethal of all urological malignancies. In 2008, Globocon worldwide survey of cancer incidence estimated 271 thousand cases of kidney tumour including RCC.[1] The American cancer society listed kidney tumours among the 6 most commonly occurring malignancies in males in developed countries,[2] while it ranked as the 11th most common occurring cancer in males worldwide.[1] The highest incidence and mortality from kidney cancers is recorded in the Czech Republic, while, high rates are also present in Estonia, Hungary and other European countries. Rates in African and Asian countries are consistently lower. In recent years an increase in incidence of localised tumour was recorded both in Europe [3] and in USA[4], owing to the increased detection of tumours of less than 4cm through radiological means.[5] The tumour is twice as common in men as in women, and peaks during 5th and 6th decades of life.[4]

In Pakistan, there is no nationwide unified cancer register and most hospitals maintain their own records. In a total of 50,000 tumours documented in the tumour registry data of Shaukat Khanam Memorial Cancer hospital, Lahore from 1994 to 2012, 1083 tumours involved kidney and related urinary organs. Among them 740 cases were present in male patients. Majority of these cases were in the range of 40 to 60 years of age. The hospital received 45 biopsies of renal tumours in 2012, 31 of which occurred in males (Shaukat Khanam cancer hospital cancer registry data, 2012).

The most common mode of presentation in developed countries is now incidental discovery of the tumour during abdominal scans. The early discovery of the tumour resulted in decrease in maximum dimension from 66.8 cm to 58.6 cm during a period of 1988 to 2002 in USA.[6] In Pakistan, the presentation is mainly heamaturia and lumbar pain. Incidental detection was the chief presentation in 12% of the cases in a study.[7]

Clinical Staging is the most important parameter in patient management (UICC, 2002). Localized tumours i.e. T_1 are principally managed through partial nephrectomy.[8] Studies on follow up of patients with partial nephrectomy have generally yielded good results.[8-11]

Probe – based thermo-ablative techniques can also be used on selective patients.[12]

Tumours larger than 7 cm i.e. T_2 and beyond require radical nephrectomy where every effort is made to achieve a total surgical excision. The ureter, renal vein and perinephric fat are included with the nephrectomy. Patients who have developed advanced disease i.e. T_3 / T_4 undergo radical nephrectomy as a part of the debulking therapy in addition to chemotherapy.[13]

Renal cell carcinoma was previously considered a single entity and upto 1981, WHO classified renal tumours as renal cell carcinoma and others. WHO classification of renal tumours 2004 divides renal cell carcinomas into clear cell, papillary, chromophobe, collecting duct of bellini, medullary, multilocular cystic, translocation associated, multilocular cystic, after neuroblastoma, mucinous tubular and spindle cell and unclassified types.[14]

Clear cell carcinoma is the most common histological variant constituting about 75% of all RCCs.[15] It can present as a unifocal mass, or rarely as multifocal mass in Von Hippel Lindau (VHL) syndrome presenting in either kidney with equal frequency. The tumour arises from the cortex as a protruding mass with a rounded, bosselated usually brownish surface. On cut section, the tumour is sharply demarcated from the normal, uninvolved portion of the kidney and has a pushing margin. The cut surface, is typically yellowish from the deposition of lipids and glycogen in the cytoplasm, but can show variegated appearance due to presence of areas of necrosis, myxoid degeneration, haemorrhage, calcification and cysts.[16]

The tumour cells in clear cell carcinoma are large, having an optically clear cytoplasm because of the presence of abundant glycogen and lipids which can be demonstrated by Periodic Acid – Schiff (PAS) and Oil Red O staining. Cell membranes are sharply defined with centrally placed nuclei. Nuclear pleomorphism increases with grade. The tumour is very vascular and has abundant endothelial lined vascular channels. The stroma is scanty with lymphocytic infiltration present in a few cases.[17]

Papillary renal cell carcinoma (PRCC) comprises 10 – 15% of the renal cell carcinomas with higher rate of bilaterality and multicentricity than the clear cell variant. Microscopically, it presents with complex papillary formations with stroma showing prominent lymphocytic infiltration and foamy macrophages.[17]

Comprising 5% of the total, chromophobe RCCs have large polygonal cells, well – defined cell membranes and a perinuclear halo. There are three histological subtypes of the tumour depending on the morphology of cells. These are the classical variant (with predominantly pale cells), the eosinophilic variant (predominantly eosinophilic cells) and the mixed types (both types). The cells are arranged in sheets and stain with Hale's colloid iron which shows the presence of acidic mucins.[18]

The current study explores the clinicopathological trends of renal cell carcinomas including age of presentation, signs and symptoms, greatest dimension, stage and histological subtype in Pakistan, which might help us in better understanding differences from the developed world.

MATERIALS AND METHODS

The study was conducted in the Department of Morbid Anatomy and Histopathology, University of Health Sciences, Lahore. The samples were collected from the pathology department of Punjab medical college, Department of Urology Allied Hospital, Faisalabad and Sheikh Zayed Hospital, Lahore. A total of 50 cases were selected for this study of variable ages, gender, stage, subtype and grade of RCC.

The tissues were processed in ascending grades of ethanol, cleared in xylene and impregnated by paraffin wax. All sections were stained with Haematoxylin and Eosin.

Complete gross and microscopic details were noted down in accordance to the criteria set by College of American Pathologists (CAP) guidelines. Clinical details were obtained from the hospital records.

RESULTS

The mean age of our study population was 50.16 ± 11.982 years.

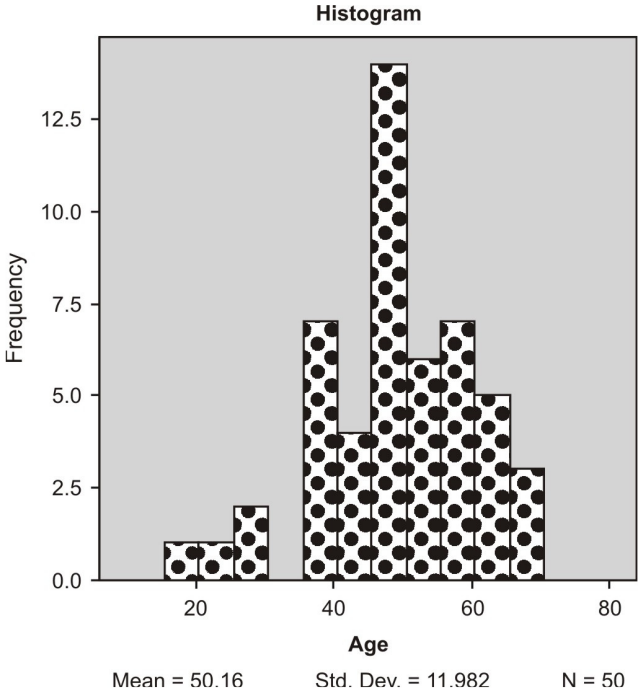

Fig. A: *Histogram showing distribution of RCC among different age groups. Note the largest number of tumours fall in 45 – 50 years category. Mean age was 50.16 ± 11.982 years.*

Regarding gender distribution, 36 (72%) of the cases were males, while the rest of 14 (28%) were females. The male to female ratio was 2.57:1. The mean age of study population in males was 51.61 ± 10.61 years as compared to 46.43 ± 17.46 years in females.

Radical nephrectomy was carried out in all the cases. Our study included no needle core biopsy speci-

men. Regarding laterality, all the cases were unilateral and the right to left ratio was 1:1. Equal number of cases (25; 50%) were present on either side.

The most common symptom was haematuria (38, 76%) followed by pain in the flanks 26 (52%) and abdominal mass 22 (44%). The classical triad (Haematuria, flank pain and mass abdomen) was found only in 16 (32%) patients. Other symptoms included weight loss, fatigue, fever, malaise, urinary retention, oedema and dysurea (Table 1).

Table 1: Signs and symptoms in (50) study patients of RCC.

Symptoms	*Present*	*Absent*	*Percentage*
Heamaturea	38	12	76
Flank Pain	26	24	52
Mass	22	28	44
Weight loss	16	34	32
Fatigue	12	38	24
Malaise	14	36	28
Fever	12	38	24
Night sweats	4	46	8
Oedema	2	48	4
Dysuria	6	44	12
Urinary retention	6	44	12

Table 1: The table shows the variable signs/symptoms in (50) patients of RCC. Note that heamaturea was the most common presenting complaint in 76% of the cases. Oedema, dysuria and urinary retention due to clots were rarely encountered. No patient in our study reported incidental detection as primary complaint.

The tumours encountered in this study were of generally large size. The greatest dimension (T) ranged from 0.1 cm to 21 cm. Mean size was 10.41 ± 4.22 cm. The mean of the greatest dimension (T) in males was 11.33 ± 3.82 cm as compared to females (8.04 ± 4.41 cm) (Fig. B).

The tumours in the current series mainly involved the upper pole in 36 (72%) cases. Tumour arising from middle of the kidney occurred in 19 (38%) cases while lower pole was involved in only 11 (22%) cases. In 10 (20%) cases there was diffuse involvement of the kidney.

In the current study most tumours advanced to Stage II (21; 42%) and Stage III (18; 36%). While 6 (12%) tumours were limited to stage I and 5 (10%) tumours fulfilled the criteria of stage IV.

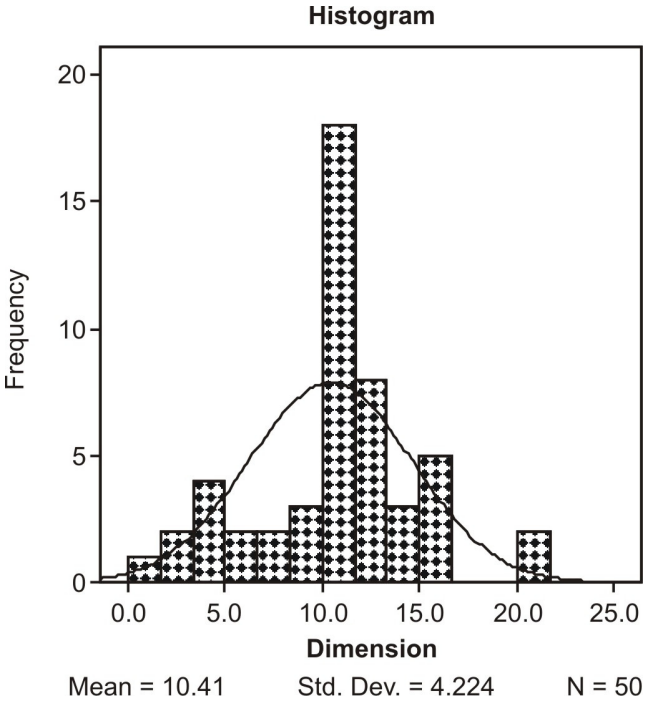

Fig. B: *Histogram showing distribution of tumours according to their greatest dimension (T). Note the largest numbers of tumours are present in 10 – 11 cm category. Normal distribution curve is drawn. Mean tumour size was 10.41 ± 4.22 cm.*

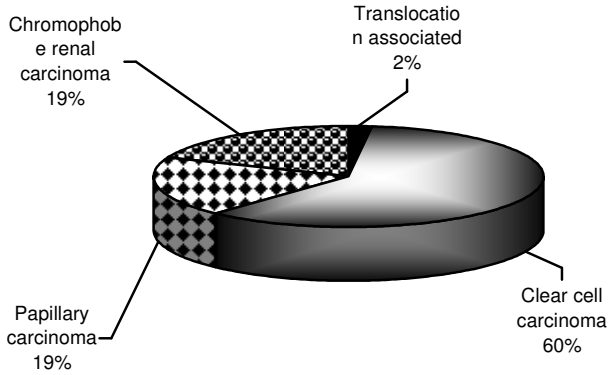

Fig. C: *Distribution of different subtypes of renal cell carcinoma.*

Fig C: Note that the clear cell carcinomas form the major proportion of renal cell carcinomas followed by papillary and chromophobe renal tumours.

The most common histological subtype present in our population was clear cell carcinoma, which was identified in 37 (74%) of the tumours. Papillary and chromophobe tumours were identified in 6 (12%) tum-

ours each. One rare translocation associated type renal carcinoma was also diagnosed.

DISCUSSION

The mean age of our patients was 50 years, although 40 (80%) of our patients were present between the ages of 37 – 65 years. The male to female ratio was found to be 2.57:1. These findings are similar to previous studies in Pakistan and showed little variation when compared with literature from other international studies.[19] However, a study by Mubarak et.al, showed almost an equal male to female ratio. This difference might be due to inclusion of only young patients in the study.[20]

The mean tumour size (T) in our study was 10.41 ± 4.22 cm which was comparable to mean (T) in Latif, et al.[15] However, most European studies mention a lower mean tumour size in the range of 5 cm.[19] The explanation is rather simple. In developed countries advances in radiological techniques has increased the detection of incidental renal tumours. In a North American study, Maxine Sun pointed out the fact that there was a yearly increase in the incidence of localised renal masses as compared to metastatic cases.[4] Incidental finding was the most common presentation in 61% of the cases in another study from the same region.[21] In contrast patients in Pakistan mostly present with haematuria and flank pain.[20] These symptoms were also the most common presentations in the current study. A substantial number of patients were initially misdiagnosed with other illnesses, such as nephrolithiasis or bladder stone. However, the current study did not take this data into account and other studies need to be done to evaluate this scenario completely.

A somewhat related issue is the stage of presentation of the tumour. In our study only 12% RCCs were limited to stage I, while 88% tumours were advanced to stage II or above. Stage II and III tumours were encountered most frequently which is in agreement with Latif, et al.[15] However, Stage I tumours were the most frequently encountered in two large European studies.[22,23]

Clear cell carcinoma was the most common subtype encountered in our study (37, 74%); and this finding is almost universal in all regional and international studies. The next most common variants were papillary (6, 12%) and chromophobe variants (6, 12%). The current study had a larger proportion of chromophobe tumours as compared to other regional and international studies.[16,22,24] A larger morphological study needs to be carried out to clearly assess the prevelance of chromophobe carcinomas.

In ***conclusion***, the lack of availability of advanced radiological techniques and the small proportion of Pakistani population which gets routine abdominal scans results in late detection of renal tumours. Most tumours are only detected when they manifest with one of the classical symptoms of the disease. In accordance with this trend tumours in our population are of larger size and have an advanced stage of presentation.

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