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Renal cell carcinoma at the time of presentation: a 5-year radiological survey at a tertiary care cancer hospital

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ABSTRACT

Background: Renal cell carcinoma (RCC) is associated with highest mortality rates of all the genitourinary tumors with increased incidence in the past few decades. It is heterogenous tumor with several histological types. Main diagnostic approach is radiological imaging followed by histopathology.

Methods: It is a retrospective study conducted at a tertiary care cancer hospital in Pakistan. We reviewed the record of all the RCC patients in terms of age, gender, radiological manifestation of tumor size, polarity, laterality, stage including nodal status, metastasis and histological type.

Results: Our study included 149 patients of RCC. Mean age of presentation was 57 years with a male predominance. The most common stage of presentation was stage 3 seen in 41% patients followed by stage 1 in 37% patients. nodal metastasis was observed in around 13% patients and distant metastasis in 8% patients. Also, majority of the patient had histological subtype of clear cell CA (63%) followed by papillary CA (33%).

Conclusions: Epidemiological features of renal cell CA are observed over a period of 5 years representing our population. The current trends show variation from those observed in developed countries depicting the struggle of healthcare awareness in developing countries.

Keywords: Carcinoma, Epidemiology, Metastasis, Renal cell carcinoma, Stage

INTRODUCTION

Renal cell carcinoma (RCC) is the most common malignancy of kidney in adults accounting for 90 percent of all the tumors arising from kidney and is associated with highest mortality rate among all the genitourinary tumors. It is a primary malignant adenocarcinoma arising from renal epithelium and shows a diversity in its histology. On the basis of histology, the most common type is clear cell carcinoma accounting 75 to 80 percent. Other types include papillary, chromophobe and collecting duct RCC from higher to lower in occurrence. Around 85% tumors arise from renal cell parenchyma and rest arise from renal pelvis. The most common age of

presentation ranges from 50 to 70 years, with increased incidence as the patients' age with male predominance.⁴ Most of the patients (60%) present with hematuria, flank pain and mass in the flank.⁵ The diagnosis is reached after combining clinical, radiological and histopathological approach. Treatment options include complete or partial nephrectomy, radiofrequency or cryoablation, depending upon the age of patient, stage of disease and other comorbidities.⁶

The incidence of RCC has been increased in the past few decades by 3 to 4 percent.⁷ It has been attributed to increased use of imaging leading to incidental detection besides the increasing risk factors.⁸ Ultrasound was used

as a screening imaging technique, but it has very low sensitivity and specificity as compared to computed tomography (CT) or magnetic resonance imaging (MRI).⁹ Both non-contrast and contrast enhanced CT scans is used as a gold standard to diagnose and stage RCC. It appears as a heterogenous hyper vascular mass often associated with necrosis and calcification.¹⁰ The TNM staging of RCC includes size of tumor, nodal involvement and metastatic spread. In T1 and T2 stages, tumor is confined to the kidney, T3 involves perinephric and vascular involvement where as T4 involves adrenal or stricture beyond Gerota's fascia. The staging of disease is the key determinant of its prognosis with a 90% 5-year survival rate in stage 1 to 5% 5-year survival rate in stage 4.¹¹

In this study authors aim to determine the spectrum of presentation of RCC on CT scan in a tertiary care cancer hospital in Pakistan at the time of diagnosis in study population.

METHODS

It was a retrospective cross-sectional study conducted at radiology department, Shaukat Khanum Cancer and Memorial Hospital, Lahore over a span of 5 years.

Inclusion criteria

All the diagnosed patients of RCC on histopathology presented from January 2015 to December 2019 were included and adult patients more than 17 years of age of both genders diagnosed with RCC on histopathology were included.

Exclusion criteria

Pediatric patients and those with incomplete record on data base were excluded, patient who received any chemotherapy treatment prior the imaging scan acquisition were also excluded.

After taking permission from the institute review board, the previous data of patients presenting with RCC diagnosed on histopathological analysis were reviewed. Patients' presenting complaints and previous medical and treatment history were assessed keeping confidentiality of all the records. The contrast enhanced CT of the chest, abdomen performed on 64 slice Toshiba scanner and 160 slice Cannon scanners of each patient were analyzed in detail including tumor size, location, invasion, lymph node involvement and metastatic lesions. Two experienced radiologists were taken on board to minimize observational bias. TNM staging was done following American Joint Committee on Cancer protocols seventh edition. Findings obtained for each patient were correlated with histopathological report for formulation of study results.

Statistical analysis

Data analysis was done using SPSS version 21 using inferential and descriptive analysis.

RESULTS

A total of 149 patients were diagnosed with RCC taking histopathology as gold standard following the inclusion criteria. The mean age of presentation was 57.12 years with a standard deviation of 9.539. The most common age group of RCC presentation was 60 to 70 years. A total 104 (69.8%) patients were male and 45 (30.2%) patients were female with a male to female ratio of 2.3:1 showing a male predominance. The distribution of data according to age of presentation is presented in the Figure 1.

Most of the tumors were located in upper pole (36.9%) and in around 142 (95.3%) patients, tumor appeared as a single unilateral mass. The majority (40.9%) of the patients has tumor masses of size 4.1 to 7 cm. The details of tumor characteristics are illustrated in Table 1.

Table 1: Representation of various tumor characteristics.

Laterality	77	C14	C4	%	
RCC size Bilateral 1 focus in each kidney More than 2 foci unilateral 1 0.70	Variables	Subset	Count		
Cach kidney	Laterality		1	0.70	
More than 2 foct unilateral 1 0.70			5	3.40	
Lower 23 15.40 lower + mid 10 6.70 Mid 25 16.80 Upper 55 36.90 Upper + mid + lower 7 4.70 Upper mid 29 19.50 Less than 4 cm 21 14.10 4.1 to 7 cm (T1a) 62 41.60 7.1 to 10 cm 42 28.20 More than 10 cm 24 16.10 Chromophobe 4 2.70 Clear cell 94 63.10 Collecting duct 2 1.30 Papillary cell 49 32.90 Nodal N1 19 12.8 Status No 130 87.20 Metastasis Absent 137 91.90 Present 12 8.10 Stage II: T2 N0 M0 18 12.10			1	0.70	
Polarity		Single unilateral	142	95.30	
Mid 25 16.80 Upper 55 36.90 Upper + mid + lower 7 4.70 Upper mid 29 19.50 RCC size Less than 4 cm 21 14.10 4.1 to 7 cm (T1a) 62 41.60 7.1 to 10 cm 42 28.20 More than 10 cm 24 16.10 Chromophobe 4 2.70 Clear cell 94 63.10 type Collecting duct 2 1.30 Papillary cell 49 32.90 Nodal N1 19 12.8 status No 130 87.20 Metastasis Absent 137 91.90 Present 12 8.10 Stage II: T1 N0 M0 54 36.20 Stage III: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90		Lower	23	15.40	
Upper		lower + mid	10	6.70	
Upper	D-1	Mid	25	16.80	
Upper mid 29 19.50	Polarity	Upper	55	36.90	
Less than 4 cm 21 14.10 4.1 to 7 cm (T1a) 62 41.60 7.1 to 10 cm 42 28.20 More than 10 cm 24 16.10 Histological type Chromophobe 4 2.70 Clear cell 94 63.10 Collecting duct 2 1.30 Papillary cell 49 32.90 Nodal status N1 19 12.8 No 130 87.20 Metastasis Absent 137 91.90 Present 12 8.10 Stage I: T1 N0 M0 54 36.20 Stage III: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90		Upper + mid + lower	7	4.70	
RCC size 4.1 to 7 cm (T1a) 62 41.60 7.1 to 10 cm 42 28.20 More than 10 cm 24 16.10 Histological type Chromophobe 4 2.70 Clear cell 94 63.10 Collecting duct 2 1.30 Papillary cell 49 32.90 Nodal status No 130 87.20 Metastasis Absent 137 91.90 Present 12 8.10 Stage I: T1 N0 M0 54 36.20 Stage II: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90		Upper mid	29	19.50	
The following colors The following colors		Less than 4 cm	21	14.10	
7.1 to 10 cm	DCC sine	4.1 to 7 cm (T1a)	62	41.60	
Chromophobe 4 2.70 Clear cell 94 63.10 Collecting duct 2 1.30 Papillary cell 49 32.90 Nodal N1 19 12.8 status No 130 87.20 Metastasis Absent 137 91.90 Present 12 8.10 Stage II: T1 N0 M0 54 36.20 Stage III: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0	RCC size	7.1 to 10 cm	42	28.20	
Histological type Clear cell 94 63.10 Papillary cell 49 32.90 Nodal status N1 19 12.8 Metastasis Absent 130 87.20 Present 12 8.10 Stage I: T1 N0 M0 54 36.20 Stage II: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90		More than 10 cm	24	16.10	
type Collecting duct 2 1.30 Papillary cell 49 32.90 Nodal status N1 19 12.8 Modal status No 130 87.20 Metastasis Absent 137 91.90 Present 12 8.10 Stage I: T1 N0 M0 54 36.20 Stage II: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90		Chromophobe	4	2.70	
Papillary cell 49 32.90 Nodal N1 19 12.8 status No 130 87.20 Stage II: T2 N0 M0 18 12.10 Stage II: T3 or N1 with M0 M1 32.90	Histological	Clear cell	94	63.10	
Nodal status N1 19 12.8 Metastasis Absent 130 87.20 Present 137 91.90 Present 12 8.10 Stage I: T1 N0 M0 54 36.20 Stage III: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90	type	Collecting duct	2	1.30	
status No 130 87.20 Metastasis Absent 137 91.90 Present 12 8.10 Stage I: T1 N0 M0 54 36.20 Stage II: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90		Papillary cell	49	32.90	
Metastasis Absent Present 137 91.90 Stage I: T1 N0 M0 54 36.20 Stage II: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90	Nodal	N1	19	12.8	
Metastasis Present 12 8.10 Stage I: T1 N0 M0 54 36.20 Stage II: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90	status	No	130	87.20	
Stage III 8.10 Stage I: T1 N0 M0 54 36.20 Stage II: T2 N0 M0 18 12.10 Stage III: T3 or N1 with M0 61 40.90	N/ -44	Absent	137	91.90	
Stage II: T2 N0 M0 18 12.10 Stage Stage III: T3 or N1 with M0 61 40.90	Metastasis	Present	12	8.10	
Stage Stage III: T3 or N1 with M0 61 40.90	Stage	Stage I: T1 N0 M0	54	36.20	
with M0		Stage II: T2 N0 M0	18	12.10	
Stage IV: T4 or M1 16 10.70		_	61	40.90	
		Stage IV: T4 or M1	16	10.70	

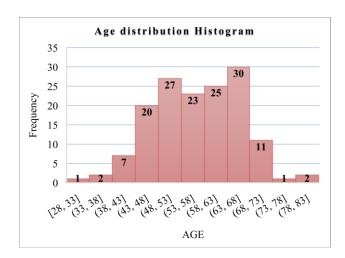


Figure 1: Age distribution of patients presenting with RCC.

The most common stage of presentation was stage 3 (T3 or N1 with M0) including 61 (40.9%) patients followed by stage 1 (T1 N0 M0) seen in 54 (36.2%) patients. However, stage 4 was present in 16 (10.7%) patients. 6 cases with IVC involvement was reported. Nodal involvement was present in 19 (12.8%) patients and metastasis was seen in 12 (8.1%) patients of which the most common site was lung followed by liver and bone as shown in Table 2.

The local invasion of the tumor was correlated with the regional nodal involvement as well as metastasis. It was noted that the patients having higher local tumor invasion showed more nodal involvement and metastasis showing a p value of <0.01 making the correlation statistically significant. Also, it was seen that metastasis was seen in all the patients with collecting duct CA and no distant metastasis was observed in chromophobe subtype of RCC shown in Table 2.

Table 2: Representation of nodal involvement and metastasis in different local tumor spread variable groups as well as in histological types.

Variables with subsets		Nodal status			Metas	Metastasis				
		N1		No		Absent		Pres	Present	
		Count (%)		Count (%)		Count (%)		Cou	Count (%)	
Renal sinus fat	Absent	6	(31.6)	80	(61.5)	85	(62.0)	1	(8.3)	
invasion	Present	13	(68.4)	50	(38.5)	52	(38.0)	11	(91.7)	
Perirenal fat	Absent	10	(52.6)	124	(95.4)	127	(92.7)	7	(58.3)	
invasion	Present	9	(47.4)	6	(4.6)	10	(7.3)	5	(41.7)	
Renal vein invasion	Absent	12	(63.2)	119	(91.5)	126	(92.0)	5	(41.7)	
	Present	7	(36.8)	11	(8.5)	11	(8.0)	7	(58.3)	
Infra diaphragmatic IVC	Absent	17	(89.5)	127	(97.7)	135	(98.5)	9	(75.0)	
	Present	2	(10.5)	3	(2.3)	2	(1.5)	3	(25.0)	
supradiaphragmatic IVC invasion	Absent	18	(94.7)	130	(100)	137	(100)	11	(91.7)	
	Present	1	(5.3)	0	(0.0)	0	(0.0)	1	(8.3)	
Ipsilateral adrenal gland involvement	Absent	16	(84.2)	126	(96.9)	133	(97.1)	9	(75.0)	
	Present	3	(15.8)	4	(3.1)	4	(2.9)	3	(25.0)	
Gerotas fascia involvement	Absent	16	(84.2)	129	(99.2)	136	(99.3)	9	(75.0)	
	Present	3	(15.8)	1	(0.8)	1	(0.7)	3	(25.0)	
Histological type	Chromophobe	0	(0.0)	4	(100)	4	(100)	0	(0.0)	
	Clear cell	11	(11.7)	83	(88.3)	85	(90.4)	9	(9.6)	
	Collecting duct	2	(100)	0	(0.0)	0	(0.0)	2	(100)	
	Papillary cell	1	(2.0)	48	(98.0)	48	(98.0)	1	(2.0)	

Figure 1, contrast enhanced CT scan axial slice showing an exophytic heterogeneous solitary left renal midpole lesion which is well confined within the renal capsule without any invasion into the renal sinus fat or fascia Gerota. Incidental finding of hepatic haemangioma in segment 6 of the liver is also noted.

Figure 2, contrast enhanced CT scan coronal section shows heterogeneous tumor almost completely replacing the right kidney with extracapsular extension as well as extension into the renal sinus fat with frank infiltration of the ipsilateral renal vein. The tumor can be seen extending into the infra-diaphragmatic IVC views

reaching up to the level of the intrahepatic IVC. The infrarenal IVC is also involved.

Figure 3, axial slice of contrast-enhanced CT scan showing heterogeneous solid masses involving the both kidneys with possible involvement of renal sinus fat on both sides.

Figure 4, depicting coronal sections through the CT scan in lung windows showing multiple solid masses scattered in the bilateral lungs in background of renal cell carcinoma suggestive of pulmonary metastases in this patient.

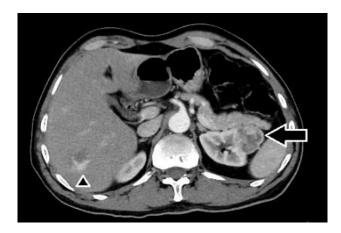


Figure 1: Contrast enhanced CT scan axial slice of an exophytic heterogeneous solitary left renal midpole lesion.

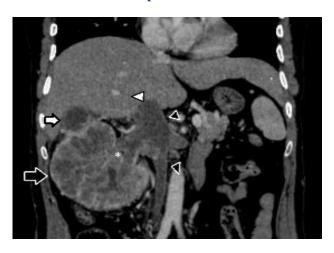


Figure 2: contrast enhanced CT scan coronal section showing locally infilterating right renal tumor.



Figure 3: Axial slice of contrast-enhanced CT scan.

Figure 5, contrast enhanced CT scan axial slice showing a necrotic nodule in the left adrenal gland in background of ipsilateral renal cell carcinoma. It is noncontiguous involvement of the adrenal gland suggestive of metastasis.

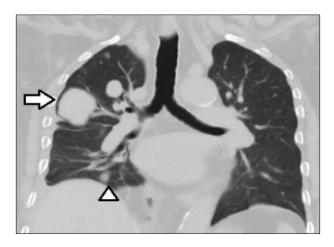


Figure 4: Coronal sections through the CT scan in lung windows with pulomnary metastasis.



Figure 5: Contrast enhanced CT scan axial slice showing a necrotic nodule in the left adrenal gland compatible with metastatic deposit.



Figure 6: Contrast enhanced CT scan axial slice showing a huge heterogeneous left renal tumor.

Figure 6, contrast-enhanced CT scan axial slice shows a heterogeneous left renal tumor completely replacing the left kidney extending beyond the fascia Gerota with involvement of the left paraspinal muscles. Multiple

enlarged necrotic para-aortic lymph nodes are also seen. Note is made of a heterogeneous relatively well-defined lesion seen in the liver segment 5 highly suggestive of hepatic metastasis.

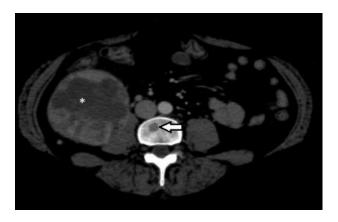


Figure 7: Contrast enhanced CT scan axial slice in bone windows showing osseous metastasis.

Figure 7, a well-defined lucent lesion seen in L4 vertebral body in background of right renal cell carcinoma at lower pole partly covered in the current slice. The scan represents a osseous metastatic deposit in background of renal cell carcinoma in this patient.

DISCUSSION

Renal cell carcinoma has shown increased incidence in the past few decades particularly in developed countries like China, Africa, India and North America. It is ranked as 13th most common malignancy all over the globe and the most malignancy of kidney. The increased use of imaging modalities has resulted into high incidence of RCC in the recent era. However there is a scarcity of epidemiological data regarding RCC in our country. In this study, we have tried to highlight the demographic features and initial presenting stage on radiological imaging of this commonly occurring malignancy in tertiary care cancer hospital Pakistan.

This study has shown that the most common age group of presentation of RCC is 60 to 70 years followed by 50 to 60 years with a male to female ratio 2.3:1. Only 4 patients presented below the age of 40 years. All the age groups showed male predominance. The mean age of presentation was 57 years. RCC is a malignancy of middle age to elderly age, with the most common age of presentation as 50 years with a male predominance in a study done by Agnihotri et al.¹³ A recent study done in Australia has also provided a male to female ratio of 2:1.14 Another study done by Gillett et al, has shown that median age for RCC diagnosis is 60 to 65 years. The incidence increases with age and only 5% patients of RCC belong to age less than 40 years.¹⁵ Similarly a study done by Jun et al in China provided a male predominance by 2.5:1 male to female ratio.¹⁶

Majority of the patients (36.9%) presented with tumor mass in upper pole, followed by upper mid pole with 19.5% patients and middle pole presentation is seen in 16.8% patients. Around 7 (4.7%) patients presented with masses in all upper, middle and lower poles. Also, laterality was significantly unilateral with 142 (95.3%) patients presented with it. However, 5 (3.4%) patients have a bilateral mass with single focus each. This is in accordance with the study done by Krambeck et al with only 2.1 percent patients had bilateral RCC.¹⁷

The size of the tumor at initial presentation was assessed in a categorical way by making four groups. Most of the patients (40.9%) had a tumor size ranging from 4.1 to 7 cm followed by tumor size of 7.1 to 10 cm consisting of 28.2% patients. However, 14% patients presented with tumor size of less than 4 cm and 16% patients had more than 10 cm lesion. In a study done by Hashim et al in Southern Pakistan, the mean size of tumor was 7.2 cm which is in agreement with our study having a mean size of 7.1 cm in all the patients. A study done in India by Agnihotri S et al, has presented the figure 8.08 cm as mean size of tumor and only 10.4% patients presented with tumor size less than 4 cm showing the late presentation with increased local spread.

In this study, renal vein invasion was present in 18 (12%) patients and 6 (4.02%) patients had inferior vena cava involvement. A study done by Latif et al, has shown renal vein involvement in 17% of their patients. Another study done by Zini et al manifested the renal vein involvement in 10.4% cases and IVC involvement in only 2.8% cases. The observations supporting aggressive nature of tumor including venous involvement is in concordance with some studies in literature.

Distant metastasis and nodal involvement are associated with higher stage of the tumor. Around 19 (12.8%) showed nodal involvement and 12 (8.1%) patients have distant metastasis which is in accordance with the study done by Négrier et al.²² The most common metastatic site observed in all the included patients was lung. Second most commonly involved site of metastasis was bone followed by liver. A study done by Umer et al is in agreement with our results of metastatic sites.²³

The determination of the stage of RCC has immense prognostic role. The treatment mode and survival rates are solely dependent on stage of the disease. The patients with localized tumor have a 5-year survival rate of 92%, whereas those presenting at stage 4 with distant metastasis has only 12% 5-year survival rate.²⁴ The majority of patients presented at stage 3 having a prevalence 41%. This late presentation is associated with several factors including low socioeconomic status, low literacy rate and lack of health facilities in rural areas. A study done by Hoch in United States has shown that around 54% patients presented at stage 1 and 2 representing the localized tumor, 21% presented at stage 3 and 25% patients presented at stage 4.¹⁹ A study done in

India has shown that most prevalent stage in .the patients of RCC presenting to them was stage 2 seen in 45.5% patients.²⁵ Different stages prevalence is seen in literature showing variations among developed and under developed countries indicating the health awareness, basic health facilities and socioeconomic status in the country.

The most commonly occurring histological subtype is clear cell carcinoma constituting 63% of all patients, followed by papillary cell CA in 33% of the patient. Collecting duct CA appeared in only 1.3% patients making it the rarest histological subtype. The results are in accordance with the study in which clear cell CA was seen 70% of the patients.²⁶

Metastasis development in RCC is incurable and associated with 50% decrease in the survival rate despite the local invasion.²⁷ Even after the removal of the local tumor in nephrectomy, more than 50% of the RCC patients develop metastasis.²⁸ In this study, a correlation was established between local invasion of the tumor and nodes and metastasis development. The results depict that more the local aggressive nature of the more, more is the nodal involvement and metastasis. So, the tumor showing increased local invasion should be followed up vigilantly for the metastasis development as the primary stage of the disease is a risk factor for metastasis as given in a study done by Edge et al. Also, the nodal metastasis is a presumptive of distant metastasis as shown in their study.^{28,29}

Metastasis and histological type have shown a pattern observed commonly in literature review. In clear cell CA, nodal metastasis was present in 11% patients and distant metastasis in 9.6% patients. Similar results are depicted in a study done by Feltrin et al.³⁰ In the duration of study, authors had only 2 patients of collecting duct and both of them showed nodal and distant metastasis. However, a study done by Tokuda in japan has reported 32% patients presenting with collecting duct CA has developed distant metastasis at initial presentation.³¹

In this study authors have highlighted major epidemiologic features, radiological presentation and histological types of RCC presenting at one of the largest tertiary care cancer hospital in our country. Authors presented a 5 years data of RCC patients including 149 patients which is the strength of this study. No such studies have been presented lately from our country.

CONCLUSION

Authors have described different epidemiological trends of initial presentation of RCC in study population that depicts presentation at advanced stages, nodal and distant metastasis as compared to developed countries. Early age and advanced stage presentation are due to lack of basic health facilities, poverty and low literacy rate. Although this single institute-based study cannot be a true

representative of study population however it can be used as a presumptive of epidemiological features and a reflection of changing trends in our country.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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