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Clinicopathological Pattern and Outcome of Early and Late Onset Renal Cell Carcinoma: An Observational Study

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ABSTRACT

Introduction

Renal cell carcinoma (RCC) is considered a disease of old age and is typically found in the 6th-8th decade of life. The diagnosis of RCC is increasing more rapidly in younger age patients. This study was conducted to evaluate the clinicopathological pattern and outcome of early onset RCC and compare them with the older age group patients.

Methods

This was a single center observational study. All the patients undergoing radical or partial nephrectomy during the period of November 2019 to October 2022 for renal masses and whose final histopathology report showed RCC were included in the study. Clinicopathological patterns and outcome were compared between the two age groups.

Results

Among 47 patients, 17 (36.2%) patients were at or below the age of ≤46 years and 30 (63.8%) patients in older age group. There was significant difference in male (29): female (18) ratio between the two age groups ($p < 0.005$). Younger age patients (≤46 yrs) had higher stage of disease at presentation compared with the older age (>46 yrs) patients [tumor extension into major veins and perinephric tissue (T_3) and above 26 vs 21] and they had significantly higher mortality rate (29.4% vs 3.3%, p =0.01).

Conclusion

Patients aged ≤46 years of age were more frequently affected by RCC with female predominance. Younger age group had higher stage of disease at presentation with higher mortality in comparison to older age group.

Keywords

Clinicopathological; early onset; late onset; outcome; renal cell carcinoma

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INTRODUCTION

Renal cell carcinoma (RCC) is the most common cancer arising from kidney and accounts for almost 90% of kidney cancers. It has diverse clinical manifestations. One of the distinguishing characteristics of RCC is its resistant to chemotherapy and radiotherapy.[1] The classic triad of flank pain, mass and hematuria known as late triad is present in 10% patients and is usually indicative of advanced disease. It usually remains asymptomatic until late in the disease, and almost 50% of tumors may be detected on incidental radiological imaging.[2]

The usual age of presentation of RCC is 6th to 8th decades of life, the median age at diagnosis being 64 years. Men are affected twice as common as female.[3] In general the disease is rare in children and uncommon in adults under the age of 46 years.[4] A recent study by Shuch et al using the SEER database, the mean age of patients was 64 years with distribution closely approaching normalcy and bottom decile cutoff was 46 years. Hence defined the age cut off for early onset RCC as 46 years, allowing clinicians a threshold for possible genetic evaluation.[5]

Currently data regarding the early onset RCC patient population is limited. We did not find any published literature regarding early and late onset of RCC. Our aim was to investigate the clinical and pathologic characteristics and outcome within this subset of patients with RCC and compare them with standard age group patients.

METHODS

This is a single institution based retrospective observational study conducted in Department of Urology and Kidney Transplant Surgery, Tribhuvan University Teaching Hospital. The study duration was three years from November 2019 to October 2022. All patients with renal masses that were clinically and radiologically suspected to be malignant and had undergone surgery were assessed for eligibility. All proven malignancy cases were included in the study. Patients with the benign histology or malignant tumors other than RCC and those with missing/incomplete data were excluded.

Study variables were age, gender, tumor size, location, TNM stage, histopathological subtypes, lymph nodes involvement, renal vein and inferior vena cava (IVC) thrombus, and survival. Staging and grading assigned according to the updated staging system by the American Joint Committee on Cancer.[6,7]

Data was retrieved from the patient's record files and proforma was used for data collection. Follow up visit data was retrieved on an outpatient basis according to staging, histopathology report and as per protocol. Follow -up duration was the total duration from the day of surgery to the last follow up or date of death.

Data were entered into Microsoft Excel sheet and then analyzed using IBM SPSS Statistics version 26. Mean and standard deviation were used for numerical variables and percentage for categorical variables. Student's independent sample's t-test was used to compare normally distributed numerical variables and Chi-square test or Fisher's exact test for unpaired proportions as appropriate. p-value ≤0.05 was considered statistically significant

The study was approved by the Institutional Review Committee of Institute of Medicine, [Ref. 310 (6-11) E2].

RESULTS

During the study period, a total of 58 patients were operated with pre-operative diagnosis of RCC. Among them benign disease and malignant disease other than RCC were seen in histopathology of four patients. In the final study total of seven patients

Table 1. Epidemiological and clinical characteristics of renal cell carcinoma patients

Characteristics		Early onset group (≤46 yrs)	Late onset group (>46 yrs)	p value
Total patients		17 (36.20)	30 (63.80)	-
Sex ratio (M:F)		6:11 (0.54)	23:7 (3.28)	<0.005
Clinical presentation	Incidental	7 (41.17)	14 (46.67)	0.72
	Symptomatic	10 (68.83)	16 (63.33)	-
Symptoms	Hematuria	5	7	0.65
	Pain	9	12	0.39
	Mass	4	1	0.03
	Wt loss	3	3	0.45

Table 2. Tumor characteristics and surgical procedure

Characteristics		Early onset group (≤46 yrs)	Late onset group (>46 yrs)	p value
Mean tumor size (cm)		7.6±3.5	7.07±3.8	0.71
Laterality	Right	8 (47.05)	15 (50)	0.85
	Left	9 (52.95)	15 (50)	
Tumor location (pole)	Upper	6	9	0.39
	Middle	2	6	
	Lower	7	9	
	>1 pole	2	6	
Procedure	Open radical nephrectomy with/without thrombectomy	16 (94.11)	23 (76.67)	0.47
	Lap radical nephrectomy	1	5	
	Partial nephrectomy	-	1	
	Lap conversion to open	-	1	

were excluded for incomplete data. Total of 47 patients were included in the final study. Twenty nine (62%) were male and 18 (38%) were female. Total number of patients in early onset age group were 17 (36.2%) of which six were male and 11 were female [Table 1]. The median age of presentation in early onset group was 36 years. Similarly total number of patients in older age group were 30 (63.8%), of which 23 were male and seven were female. The median age of presentation was 62 years.

Most of the renal masses were diagnosed incidentally and the rate of detection was similar in both the groups. In symptomatic patients, incidence of hematuria, flank pain, weight loss were similar in both groups but the detection of mass during clinical examination finding was significantly more in early onset group of patients (p=0.03). The classic triad of flank pain, mass and hematuria was present in two patients. Smoking was more common in male patients as compared to female patients (p=0.03), and in older age group patients in comparison to early onset age group (p= 0.05).

Mean tumor size, laterality, and tumor location were similar between the two groups [Table 2]. Most of the cases were operated via open surgical approach.

Histopathologically, patients <46 yrs of age were found to have more advanced stage of the disease as compared to that of older age group[tumor limited to kidney (pT_1-$2N_0M_0$) 47.05% vs 56.67% p = 0.22]. Most common histopathological variant was clear cell carcinoma followed by papillary RCC in both the groups [Table 3].

Table 3. Staging and histological subtypes

Characteristics		Early onset group (≤46 yrs)	Late onset group (>46 yrs)	p value
Staging	pT_1+T_2 N_0M_0	8 (47.05%)	17 (56.67%)	0.22
	pT_3	9	9	
	pT_4/N_1-N_2 and/or M_1	-	4	
Histology	Clear cell	11 (64.7%)	22 (73.33%)	0.13
	Papillary	4	4	
	Chromophobe	-	1	
	Sarcoma	2	1	
Tumor thrombus		3	9	0.35
Recurrence		3	3	0.45
Mortality		5	1	0.01

There were total of 12 cases of tumor thrombus in renal vein and IVC. Presence of tumor thrombus didn't influence the recurrence, but it was an independent risk factor for mortality (p=0.01). Four out of 12 patients with tumor thrombus died of the disease.

There was no difference in average hospital stay in both the age groups. The average hospital stay in early onset age group was 5.53±2.62 days and 5.17±2.16 days in older age group patients. Post operative fever, superficial surgical site infection, urinary tract infection were few of minor complications following radical/partial nephrectomy and they were similar between the two age groups.

Total of six patients had recurrence of disease and it was similar in both groups with three patients in each group over mean follow up period of 20.88 months in early age group and 22.51 months in older age group. Similarly, a total of six patients died of RCC, five in young age group and one in older age group having statistical significance (p=0.01) [Table 3].

DISCUSSION

RCC is generally considered a disease of old age, although data from developing country like Nepal are lacking. Studies from developed countries have shown that the incidence of early onset RCC is around 15-20%, while in our study 36.17% of patients were at or below the age of 46 yrs.

The histological subtypes of RCC in our study matched with the previous studies.[8] The predominant histological subtype was conventional clear cell RCC followed by papillary RCC in both the age groups with similar incidence. Hereditary RCC are associated with an earlier age of onset and may be associated with syndromic or genetic component or family history of RCC, however its incidence is low.[9] In a study by Gordetsky J et al. involving 576 patients with RCC, they found that only two patients with early onset RCC had family history of RCC and neither of the patients had bilateral disease.[10] In our study also there was no family history of RCC and neither of patients had bilateral disease.

In general the male: female ratio in RCC is almost 1:2. In our study the ratio of male: female ratio in patients <46 years was significantly low with female predominance. Various other studies have also shown low male: female ratio among patients of younger age group.[11]

Most of previous studies involving early onset RCC patients were found to have lower stage tumors and were also more likely to undergo a partial nephrectomy.[10] Our study showed that younger patients were more symptomatic than the older age patients and they had higher tumor stage as compared to the older age group although both the results were not statistically significant. Partial nephrectomy was less frequently performed at our center for RCC. The possible explanation for this could be due to relatively larger tumor size and higher stage at presentation. In our study, 81% of tumors were >4 cm with mean tumor size of 7.26±3.31 cm.

There was no difference in recurrence of the disease between two groups. Mortality rate was significantly higher in early onset age group. This higher mortality observed in early onset age group could be due to higher stage at presentation with more aggressive or unfavourable histological subtypes. This finding is in contradiction to what has been found in literature. In a study conducted in the Department of Pathology, Alabama University, the authors found low recurrence of disease with low mortality (4.2%) in early onset age group with excellent prognosis.[10]

This is a retrospective study so it relies on the information available in the medical records which may not be sufficient. The sample size is relatively small with short duration of follow up.

Further studies including large population with longer duration of follow up probably in prospective set up would project the actual scenario of renal cell carcinoma with reference to the age.

CONCLUSION

Most common presentation of RCC was incidental finding but early onset tumors were more likely to be symptomatic and higher stage than late onset tumors. Early onset tumors were more common in female population and had high mortality. The role of genetic counselling and germ-line mutation testing should be further explored in patients who present with RCC in early period of life.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

Study concept, design and data collection: DP; Analysis and interpretation of data: DP, AP; All authors proofread and approved the final manuscript.

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