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CLINICOPATHOLOGICAL ASSESSMENT OF RENAL TUMORS IN A SAMPLE OF ADULT IRAQI PATIENTS

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ABSTRACT

Introduction: The kidney can develop both benign and malignant neoplasms. The most deadly of all urologic cancers is renal cell carcinoma (RCC), which makes up 2% to 3% of all adult malignant neoplasms. **Method:** A cross-sectional observation retrospective analysis of 467 selected patients with kidney cancer (from 2014- 2023), which includes a retrospective analysis of 430 randomly selected patients with kidney tumors who were collected from Teaching Laboratory of Al-Sader Medical City, over the period from June 2024 to August 2024 **Results:** the total number of patients were 430 patients with renal cancer with age range (18-85 years old). Medain age was 52 years old. Male to female ratio was 1.5:1. The most frequent type of renal cancer was: first clear cell carcinoma about 298(69.3%), second papillary RCC 68(15.8%) (papillary RCC type I about 51(75%) and (papillary RCC type I 17(25%), third chromophobe RCC about 35 (8.1%). There was significant association between age and histological subtypes, also there was a weak association between grading and histological subtypes. **Conclusion:** The histological subtypes of RCC were associated with age groups and with nuclear grading. And RCC was more frequent in age groups (41-50 years) and (51-60 years).

KEYWORDS: RCC, kidney tumors, Iraqi patients. Renal cell carcinoma.

INTRODUCTION

Kidney cancer is not a single illness, but rather a collection of several cancer forms with varying presentations, clinical courses, and genetic foundations that are categorized according to their histology. Research on families affected by hereditary renal cell carcinoma (RCC) has served as a foundation for our knowledge of the genes responsible and the altered metabolic pathways in various histology of renal cancer. Von Hippel-Lindau disease was the first kidney carcinoma condition with a known genetic basis.[1]

One of the top ten malignancies that affect both male and female in the US is kidney cancer. About 4% to 5% of all malignancies are caused by it. An estimated 81,610 new cases of kidney cancer will be identified, including 29,230 in female and 52,380 in male. This disease will kill about 14,390 persons, 9,450 of them will be male and 4,940 of whom will be female. Most patients are diagnosed between the ages of 55 and 74, with an average age of 65 at diagnosis. In individuals under 45, kidney cancer is rare.[2] In the US, black people had greater incidence and fatality rates than white people.[3] In our country, The incidence rate of kidney cancer in Iraq, male 4.14 %, female 1.75%, and total incidence of kidney cancer from all cancer 2.75%.[4]

According to research, smoking, obesity, diabetes, and hypertension are common risk factors for kidney cancer.[6]

In renal cell carcinoma, clear cell carcinoma is the most prevalent histological type.[7] The ninth most prevalent cancer in males and the fourteenth most common in women is RCC.[8] A higher prevalence in recent decades has been linked to improved disease diagnosis and exposure to different risk factors.[7] The industrialized world's greatest incidence rates are seen in North America and Northern and Eastern Europe.[9]

Renal parenchyma gives rise to kidney cancer. In adults, clear cell renal cell carcinomas account for around 70% of instances of kidney cancer.[10]

This study aims to assess the correlation between histopathological diagnosis of renal tumors and various clinicopathological parameters in samples of patients from Middle Euphrates of Iraq.

METHOD

Study design and setting: A cross-sectional observation retrospective analysis of 467 selected patients with kidney cancer (from 2014- 2023), which were collected from Teaching Laboratory of Al-Sader Medical City, and private laboratories over the period from June 2024 to August 2024. The clinical parameters such as (age, gender, associated clinical features, size, side, site, tumor subtypes and grade and pathological stage), were taken from patients' data available and pathology reports.

❖ Inclusion Criteria

Adults patients with partial and radical nephrectomy operation for kidney tumors.

❖ Exclusion criteria

1. Recurrent tumor.
2. Tumor of renal pelvis.
3. Samples by core biopsy.

Data Collection

The following data were collected from all patients:

1. Demographic characteristics of patients including age, gender.
2. Histological subtypes of RCC for adults
3. Histopathological features include staging and grading for both RCC.

Ethical consideration

The confidentiality of data throughout the study was guaranteed and we were assured that data will be used for research purposes only. The issue number of our study was (Path 25).

Statistical Analysis

Data were analyzed using IBM SPSS version 24 (SPSS Inc., Chicago, Illinois, USA) and excel Microsoft office 2016. Use descriptive analyzes for frequency and percent. Numerical data were expressed as mean± standard deviation (SD) or median and range, as appropriate and analyzed with Chi square. A- P value less than 0.05 was considered significant

RESULTS

The total noumber of patients were 430 patients with renal cancer with age range (18-85 years old). Mean age was 52±13 years old. **Table 1** shows that a high percentage of patients with age group (51-60 years), about 109 (25.3%). Followed by age group (41-50 years), about 108(25.1%) .Males were more affected than females, Male to female ratio was 1.5:1. that stage I is the most frequent stage 267(62.1%), followed by stage III about 94(21.9%). shows that regarding RCC grading, RCC grading, the I, and II grades were the highest percentage, about 215(50%) and 162(37.7%) respectively. **shows** The size of RCC was in four groups, the first group (≤4) was the most predominance 163 (37.9%), and the second was (4-7 cm) about 146(34%). shows that the right kidney was slightly more affected with RCC about 172(40%). shows that the upper pole involvement was more common 47(10.9%), about 323(75.1%), not mentioned in the report paper. Just 8.8% cases were with lymph nodes availability, and only 15% was positive (Pn1) **Table 2** shows that the most frequent type of renal cancer was: first clear cell carcinoma about 298(69.3%), second papillary RCC 68(15.8%) (papillary RCC type I about 51(75%) and papillary RCC type II 17(25%), third chromophobe RCC about 35(8.1%). shows **Figure 1** shows the other histological features as the following: (88.8%) 382 of samples with single focality, for vein invasion 13(3%) and fat invasion 95(22.1). **Table 3** shows a statically significant association between histopathological diagnosis and age. P-value ≤0.001, in the age group (51-60), the most common histological type was clear cell carcinoma, with significant p-value ≤0.001. **Table 4** shows a statistically significant association was detected between tumor grade and histopathological diagnosis (P- value < 0.001); as most cases of clear cell type carcinoma were of grade I; The tumor grade I, was the most frequent with the most histological types, with significant p-value ≤0.001.

Table 1: Basic Characteristics of the Studied Sample (N = 430).

Parameter	Category	Frequency (n)	Percentage (%)
Age Group (years)	≤20	5	1.2%
	21–30	20	4.7%
	31–40	64	14.9%
	41–50	108	25.1%
	51–60	109	25.3%
	61–70	87	20.2%
	≥71	37	8.6%
Gender	Male	266	61.9%
	Female	164	38.1%
Tumor Size (cm)	≤4	163	37.9%
	4–7	146	34.0%
	8–10	85	19.8%
	>10	36	8.4%

Tumor Side	Right	172	40.0%
	Left	169	20.6%
Tumor Site	Upper Pole	47	10.9%
	Middle pole	14	3.3%
	Lower pole	36	8.4%
	Not Mentioned	323	75.1%
	Entire kidney	10	2.3%
Lymph Node Status	present	38	8.8%
	Positive (Pn1)	6	15.7% of 38
	Pn0	32	84.3% of 38
Tumor Stage	Stage I	267	62.1%
	Stage II	63	14.7%
	Stage III	94	21.9%
	Stage IV	6	104%
Tumor Grade	Grade I	215	50.0%
	Grade II	162	37.7%
	Grade III	26	6.0%
	Grade IV	27	6.3%

Table 2: Distribution of renal cell carcinoma cases.

Types	No.	%
Clear cell type carcinoma	298	**69.3**
Papillary renal cell carcinoma	68	**15.8**
Chromophobe renal cell carcinoma	35	**8.1**
Sarcomatoid type renal cell carcinoma	9	**2.1**
Mucinous tubuler spindle cell carcinoma	7	**1.6**
Clear cell papillary RCC	6	**1.4**
Multiloculer cystic renal neoplasim of low malignant potential	2	**0.5**
Other types		
Eosinophilic,solid and cystic RCC	1	**0.2**
Collecting duct carcinoma	1	**0.2**
MiT familly translocation RCC	1	**0.2**
Fumarate Hydratase Deficient RCC	1	**0.2**
Thyroid like follicular carcinoma	1	**0.2**

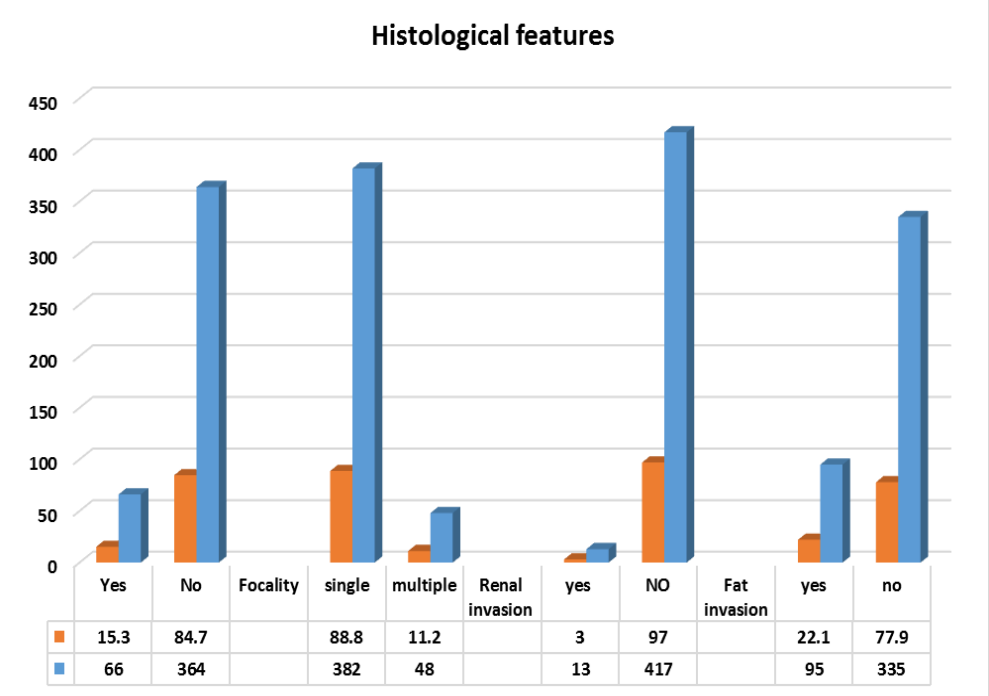

Figure 1: Distribution of other histological feature.

Table 3: Association histopathological diagnosis and age.

Histological Subtypes	Age							Total
	≤20	21-30	31-40	41-50	51-60	61-70	≥70	
Clear cell typecarcinoma	2	10	48	83	74	54	27	298
	0.7%	3.4%	16.1%	27.9%	24.8%	18.15	9.1%	100%
Papillary renal cell carcinoma	1	4	7	11	21	17	7	68
	1.5%	5.9%	10.3%	16.2%	30.9%	25%	10.3%	100%
Chromophobe renal cell carcinoma	0	5	6	11	4	7	2	35
	0.0%	14.3%	17.1%	31.45	11.4%	20%	5.7%	100%
Clear cell papillary RCC	0	0	1	2	3	0	0	6
	0.0%	0.0%	16.7%	33.3%	50%	0.0%	0.0%	100%
Mucinous tubuler spindle cell carcinoma	0	0	0	1	3	3	0	7
	0.0%	0.0%	0.0%	14.3%	42.9%	42.9%	0.0%	100%
Multiloculer cystic renal neoplasim of low malignant potential	0	0	1	0	0	1	0	2
	0.0%	0.0%	50%	0.0%	0.0%	50%	0.0%	100%
Sarcomatoid type renal cell Carcinoma	0	1	1	0	4	2	1	9
	0.0%	11.1%	11.1%	0.0%	44.4%	22.2%	11.1%	100%
Total	5	20	64	108	109	87	37	430
	1.2%	4.7%	14.9%	25.1%	25.3%	20.2%	8.6%	100%
Statistical significance (p≤0.001)								

Table 4: Association between histopathological type of malignant tumors and tumor grade.

Histopathology	Tumor grade				Total
	Grade I	Grade II	Grade III	Grade IV	
Clear cell typecarcinoma	145	128	13	12	**298**
	48.7%	43.0%	4.4%	4%	**100%**
Papillary renal cell carcinoma	25	27	13	3	**68**
	36.8%	39.7%	19.1%	4.4%	**100%**
Chromophobe renal cell carcinoma	31	3	0	1	**35**
	88.6%	8.6%	0.0%	2.9%	**100%**
Clear cell papillaryRCC	4	2	0	0	**6**
	66.7%	33.3%	0.0%	0.0%	**100%**
Mucinous tubuler spindle cell carcinoma	7	0	0	0	**7**
	100%	0.0%	0.0%	0.0%	**100%**
Multiloculer cystic renal neoplasim of low malignant potential	2	0	0	0	**2**
	100%	0.0%	0.0%	0.0%	**100%**
Sarcomatoid type renal Cell carcinoma	0	0	0	9	**9**
	0.0%	0.0%	0.0%	100%	**100%**
Total	215	16	26	27	**430**
	50.%	37.7%	6.0%	6.3%	**100.0%**
*Statistically significant P -value < 0.001					

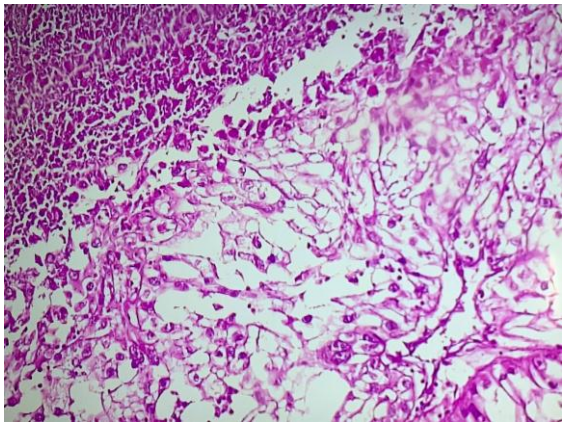

Figure 2: Section of clear cell type renal cell carcinoma showing, grade 3, and prominent thin-walled vessels, at (400x, H&E).

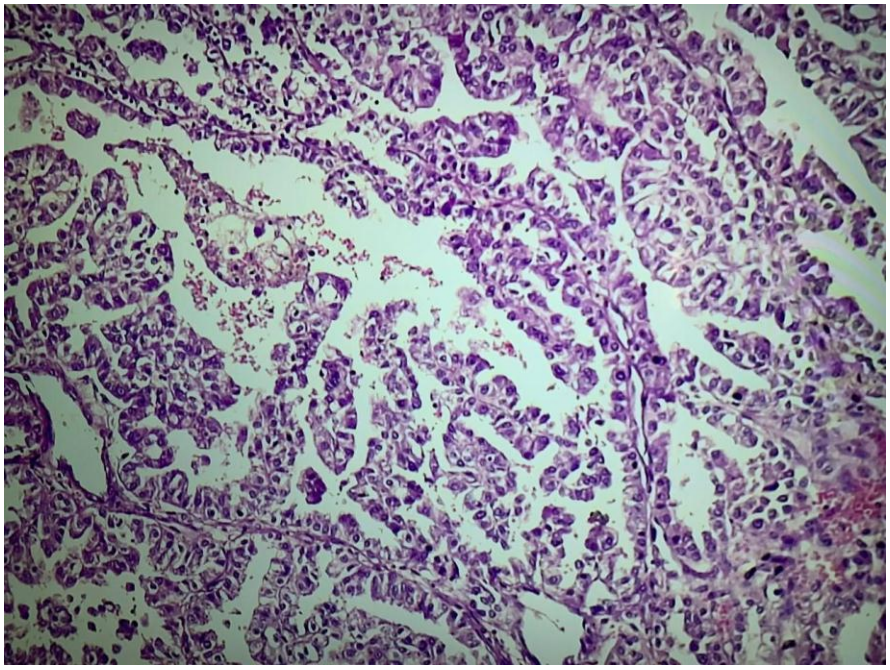

Figure 3: Section of renal cell carcinoma, (A&B) Papillary type showing tumor cells arranged in pappille lined by cells with pale cytoplasm arrenged on single layer, (at 400x, H&E).

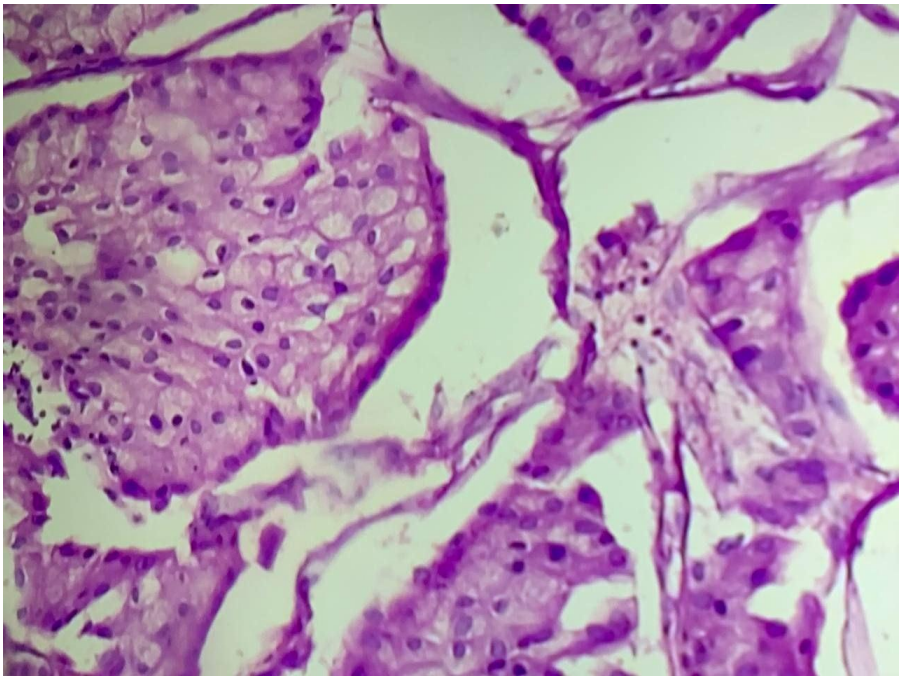

Figure 4: Section of RCC, chromophobe type, showing acidophilic granular cells with perinuclear halo (arrow), (H&E, 400x).

DISCUSSION

In our study, we found that ccRCC was more common in male 176(59.1%) and female 122(40.9%) patients, followed by papillary and chromophobe carcinoma. With age range (18-85), (Age group classification according Pallagani, L., et al (87), and its mean 52.33± 13 with significant association with RCC subtypes as P-value ≤0.001, males more than females, and for tumor size, the size ≤4 more frequent 163(37.9%). An earlier study conducted in 2017 by Wu J. et al. on Chinese patients**,** Males made up about two-thirds (67.7%) of the total patients. The renal mass's median maximal dimension (Dmax) was 4.0 cm, and the median age at diagnosis was 56 years old. 88.9% of all cases were clear-cell renal cell carcinoma, which made up the majority. Additionally, there was a significant difference in the distribution of RCC subtypes by age (P = 0.011). This finding is very similar to what we found.[11] In our study, we note that most patients presented were in the sixth decade followed by fifth then seventh decades. Recent study by Pallagani L. et al – 2021, in USA had results near to our results, RCC was identified in 142 patients in total, 104

of whom were men and 38 of whom were women. The median age at presentation was 58 years, the majority of patients were in their sixth and seventh decades, the youngest patient was 20 years old, and the oldest patient was 84 years old.[12] The present study showed that middle-aged patients have the second highest percentage 108(25.1%), and this may indicate their exposure to several factors and risks that cause a rise in the incidence of middle ages[13] Another study by Marostica E. et al- 2021, in Boston, showed the mean age between different histological subtypes of RCC, where ccRR was 759 with mean age 60.6 ± 12.2 years , pcRR was 288 with mean age 51.7 ± 13.8, and chRCC was 103 with mean age 51.7 ± 13.8 years , compared to our study, the rates of age distribution on the types were close to the two study.[14] Study by Fu, W. et al – 2016, included 544 patients (mean age – 60 years, age range – 22–88 years,) with 520 RCCs. 410 (78.8%) patients had clear cell RCCs, 78 patients (15%) had papillary RCCs, and 32 (6.2%) patients had chromophobe RCCs.[15]

About side, the right side showed a slight predominance 172(40%), , that like study done by Guo S. et al – 2019, in USA among the 41,138 patients, 50.6% had right-sided RCC. [16] The incidence of RCC is similar with right-sided and left-sided RCC.[16] Another study by Marostica E. et al- 2021, in Boston, showed that the left side has more predominance (57.42%), this difference may be due to the large difference between the number of samples between the two study.[14]

Regarding lymph node availability was 38(8.8%) and it was positive in 6(15.7%), According to a previous study by Zareba P. et al. (2019), underwent radical nephrectomy and LND, and had a median LN yield of 3 and a median number of positive LN was 1 were found in the National Cancer Data Base (NCDB).[17] Tadayoni, A. (2018) published a study found that (14.11%) had LNM. The tumor size distribution was as follows: ≤4 cm: n = 1,212 (14.62%), 4–7 cm: n = 2,278 (27.47%), 7–10 cm: n = 2,428 (29.93%), and >10 cm: n = 2,320 (27.98%). In general, all four tumor size groups were highly representative. This study evaluated the connection between LNM and tumor size. There was a strong correlation between a larger tumor and a higher risk of LNM. Patients with ccRCC who had tumors less than 4 cm had the lowest rate of LNM (3.38%), which gradually raised to 21.55% in patients whose tumors were larger than 10 cm. According to this study, there was a clear correlation between a bigger tumor size and a higher risk of LNM.[18]. Since most of the study samples are smaller than 4 cm, this explains why most lymph nodes are not involved. It is believed that hematogenous rather than lymphatic pathways are the main means by which RCC spreads. Although isolated regional LN metastases are rare in this condition, postmortem studies have revealed that over 90% of patients with retroperitoneal LN metastases also have contemporaneous visceral and/or bone involvement.[19]

Regarding grading in the current research, most were in grade I 215(50%), followed by grade II 162(37.7%), with significant association with RCC subtypes. In a retrospective study by Ahmed F. et al. (2022), in Bangladesh, indicated that the majority of renal cell carcinoma subtypes had Fuhrman nuclear grades 2 and 3, which were strongly associated with RCC subtypes.[20] This discrepancy results from varying sample sizes. Monda, S. et al- 2023, found that localized RCC with grade II, 56 883 (51%) and grade III, 26 736 (24%) more predominance, and in patients with metastatic RCC, grade III, and grade IV were more predominance, 3658 (30%), 2390 (20%) respectively.[21]

Staging in our finding show, the stage I more predominance 267(62.1%) followed by stage III 94(21.9%) then stage II 63(14.7%), similar to finding of study in by Abdel-Rahman O. Et al – 201889,968 patients with RCC were found in this cohort; 68,318 (75.9%) had clear cell RCC, 14,791 (16.4%) had papillary RCC, and 6458 (7.1%) had chromophobe RCC. With the exception of individuals with collecting duct carcinoma, who typically arrive at a more advanced stage, the majority of patients present at an earlier stage (stage I/II). However, compared to stage I and stage III, people with stage II are less common.[22] Other previous study by Marostica, E et al-2021, found that stage I more predominance in most type of RCC, flowed by stage III then stage II, as ccRCC in stage I was 45 (43.7%) , stage II 32 (31.1%) and stage III 19 (18.4%) . pRCC stage I was 171 (59.4%) , stage II 21 (7.3%) and stage III 52 (18.1%) .chRCC 269 (50.1%) , 57 (10.6%) , 125 (23.3%) , respectively.[14] In present study, clear cell RCC, papillary RCC, and chromophobe RCC presented at early stage, while collecting duct carcinoma and sarcomatiod carcinoma presented at advance stage.

About other histological features, fat invasion 95(22.1%), renal vein invasion 13(3%), and necrosis 66(15.3). This study found was with little percentage of invasion and necrosis, because most samples was size ≤4. In previous study by Taneja et al - 2018, in USA, proven there is a correlation between increasing tumor size, clear cell histology and higher tumor grade were found to be associated significantly with retrograde venous invasion.[23] Taneja, K. (2018) found that 148 (49%) of the 300 specimens had partial nephrectomy. The interquartile range for tumor size was 2.5–6.1, with a median of 4.0 cm. Multifocal 21 (7%), extension into renal vein tributaries 52 (17%), retrograde venous invasion 15 (5%), and renal sinus invasion 40 (13%).[23]

Patients with pathologically proven pT3a RCC from radical and partial nephrectomies carried out at the Singapore General Hospital, by Chen et al – 2017, The patients with renal vein invasion had larger tumors (median, 7.2 ± 3.0 cm vs 5.5±3.6 cm, P = 0.039), and were more symptomatic.[24]

CONCLUSION

Middle-aged adults were more likely to have renal cancer, and men were more likely than women to be affected. Papillary and chromophobe subtypes were the next most prevalent histological types, after clear cell carcinoma. Most of the cases were low-grade tumors that were discovered early. The right kidney exhibited a marginally higher rate of involvement, and smaller tumor sizes were more prevalent. The most commonly reported anatomical site was upper pole localization, the majority of tumors showed single focality. Age and tumor were found to be statistically significantly correlated with histological type.

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