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CHARACTERISTICS OF RENAL CELL CARCINOMA IN PATIENTS ADMITTED TO GHAZI AL-HARIRI SURGICAL SPECIALTY TEACHING HOSPITAL, BAGHDAD-IRAQ 2020-2022

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ABSTRACT

Background: RCC is the most prevalent kidney cancer. It causes 90% of kidney cancers and 2% of adult cancers. The 2020 Iraqi Cancer Registry reported 200 new kidney cancer cases, 129 males and 71 females, with an occurrence rate of 2.97/100000 male population and 1.68/100000 female population. This research examined the epidemiology, histopathology, and staging of renal cell carcinoma patients at Ghazy AL-Hariri Surgical Specialty Teaching Hospital and identified characteristics related with advanced staging and grading. **Method:** A cross sectional study was conducted at Ghazy AL-Hariri Surgical Specialty Teaching Hospital, Medical City Health Directorate during the period from January, 2020- July 2022. All records of patients with renal cell carcinoma available during the study period were reviewed and a data collection form was prepared to collect the available data from patients' pathological records. Results: The present research comprised 100 renal cell carcinoma cases, 65 (65%) of which were male, roughly 2:1. Their mean age was 53.4 ± 10.8 years, ranging from 30 to 80. Radical nephrectomy was done on 88.0% of right kidney tumours. Most tumours were lower pole (35.0%), conventional renal cell CA/clear cell type (76.0%), and unifocal (96.0%). 8 individuals had sarcomatoid characteristics, 38 had kidney-limited tumours, and 29 had perinephric fat infiltration. Grading showed that 49.0% of patients were G2, 24.0% G3, and 62.0% pT3. 91% had no lympho-vascular invasion and all had clear surgical margins. The tumour size ranges from 1.5-20 cm with a mean of 6.7 ± 3.3 cm SD. Patients with pT2 and pT3 had larger tumours than those with pT1 (ANOVA, P<0.001), advanced staging (ANOVA, P<0.001), and grading and pathological staging were statistically significant (Fisher's Exact, P<0.001). **Conclusion:** The most prevalent type was Conventional renal cell CA/clear cell type, the majority were unifocal, 8% had sarcomatoid differentiation, and 38% were kidney-limited.9% of tumours had lymphovascular invasion and were Stage pT3 and Fuhrman Grade 2.

KEYWORDS: Characteristics, Renal Cell Carcinoma, Ghazi AL-Hariri Surgical Specialty Teaching Hospital, Baghdad, 2020-2022.

INTRODUCTION

Renal cell carcinoma (RCC) is a prevalent form of kidney cancer, accounting for 90% of all cases and affecting over 400,000 individuals worldwide each year.[1,2] It is the ninth most common cancer in American men and the fourteenth most common in women.[3] RCC diagnosis occurs more frequently in men than women and is generally diagnosed between 60 and 70 years of age.[4] RCC encompasses a variety of tumors, each with distinct histological and genetic features that resemble different parts of the nephron.[3] Advances in imaging techniques have led to a majority of renal masses being discovered incidentally. Diagnosing specific subtypes of RCC has become increasingly complex since the modern classification was introduced in 1997. Identifying subtypes is crucial due to their unique molecular correlates, immunophenotypes, and varying biological potential for aggressive behavior, as well as emerging therapeutic implications.[5] In 2022, the World Health Organization (WHO) introduced a new classification for molecularly well-defined renal tumor subtypes, which included significant changes such as the addition of certain categories and the elimination of the subcategorization of type 1/2 papillary RCC.[6] Clear cell

RCC is characterized by a nested or tubular growth pattern, with cells featuring optically clear cytoplasm surrounded by a complex capillary network. Papillary RCC typically has a classic morphology but can exhibit other appearances, including a predominant solid phenotype. Many tumors previously diagnosed as type 2 PRCC now constitute independent entities. Chromophobe RCC can have various morphologies but typically maintains CK7/CKIT co-expression, characteristic chromosomal monosomies, and a favorable prognosis.[6] Grading RCC has been validated for clear cell RCC and papillary RCC. However, validation studies for chromophobe RCC have failed to demonstrate a correlation between grade and outcome for both the superseded Fuhrman grading system and the WHO/ISUP grading classification. Consequently, it is recommended not to grade these tumors.[7] The WHO/ISUP system has been incorporated into the structured reports of the International Cancer Collaboration on Cancer Reporting for both clear cell and papillary RCC. Other types of RCC may be graded for descriptive and diagnostic purposes, but this should be emphasized in the report as not being used for outcome prediction.[7] Clinical staging is essential for determining treatment options, such as nephron-sparing surgery versus radical nephrectomy, particularly in cases of solitary kidney and decreased renal function. Pathological staging can guide clinical follow-up schedules, patient counseling, and enrollment in clinical trials. The AJCC TNM is the most recent and commonly used staging system. The five-year overall survival rate for localized disease is 92.6%, falling to 66.7% with regional nodal spread and 11.7% with metastasis.[3] Ensuring the accuracy and consistency of histopathology reports for both diagnostic and research purposes is vital, highlighting the importance of standardizing specimen handling and pathological assessment.[8,9] The main goals of this research were as follows: To describe the demographics, diagnoses, and treatments of renal cell carcinoma (RCC) patients treated at Ghazy AL-Hariri Surgical Specialty Teaching Hospital and identifying predictors of high-quality staging and grading at a later stage.

METHOD

Study Design and Setting: A cross-sectional study took place at Ghazy AL-Hariri Surgical Specialty Teaching Hospital, Medical City Health Directorate, from January 2020 to July 2022.

Study Population: The study reviewed all available records of patients diagnosed with renal cell carcinoma during the study period. Data Collection: A data collection form was designed to gather information from patients' histopathological records. The form included the following data: ¬ Age (in years), ¬ Gender, ¬ Affected kidney (right, left), ¬ Surgical operation performed (Radical Nephrectomy, Partial Nephrectomy), ¬ Histopathological features: o Tumor site: Upper, middle, lower pole, extends beyond one pole o Tumor size in centimeters o Focality: Unifocal, Multifocal o Histologic type: Conventional renal cell carcinoma/clear cell type, Papillary renal cell carcinoma-type 1, Papillary renal cell carcinoma-type 2, Renal cell carcinoma/chromophobe type o Features: Sarcomatoid, Rhabdoid, both features, not identified o Histological grade: The World Health Organization/International Society of Urological Pathology grading system for clear cell and papillary renal cell carcinoma [(10)]: ♣ Grade 1: Tumor cell nucleoli absent or inconspicuous and basophilic at 400x magnification. ♣ Grade 2: Tumor cell nucleoli conspicuous and eosinophilic at 400x magnification and visible but not prominent at 100x magnification. ♣ Grade 3: Tumor cell nucleoli conspicuous and eosinophilic at 100x magnification. ♣ Grade 4: Tumors exhibiting extreme nuclear pleomorphism, tumor giant cells, and/or any proportion of tumor displaying sarcomatoid and/or rhabdoid dedifferentiation. o Microscopic tumor extension: ♣ Tumor margins: Free, not free ♣ Lymph-vascular invasion: Identified, not identified o Pathologic staging: ♣ pT1: Tumor 7 cm or less in the greatest dimension, limited to the kidney, ♣ pT2: Tumor >7 cm in the greatest dimension, limited to the kidney ♣ pT3: Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota's fascia. This classification followed the College of American Pathologists (CAP) protocol. Data Analysis: Microsoft Excel-10 and Statistical Package for Social Sciences (SPSS) version 20 were utilized for data entry and analysis. Continuous variables were reported as mean ± Standard Deviation (SD), while categorical variables were presented as frequencies and relative frequencies. The Student t-test and Analysis of Variance (ANOVA) were used to test significant differences between means, and the Chi-Square or Fisher's Exact tests were employed to examine significant associations between categorical variables. A p-value of <0.05 was considered statistically significant.

RESULTS

Hundred Cases of renal cell carcinoma were included in the current study; 65 (65%) were males with a male to female ratio of nearly 2:1 (Figure 1). Their age ranged from 30 – 80 years with a mean of 53.4 ± 10.8 years Standard Deviation (SD). Males were slightly older than females: Males age range from 30-80 years with a mean of 53.6 ± 10.8 years SD and females age ranged from 33-70 years with a mean of 53 ± 11.1 years SD, yet the difference in mean age between males and females was statistically not significant (Student's T Test, Df= 98, P=0.78) (Table 1).

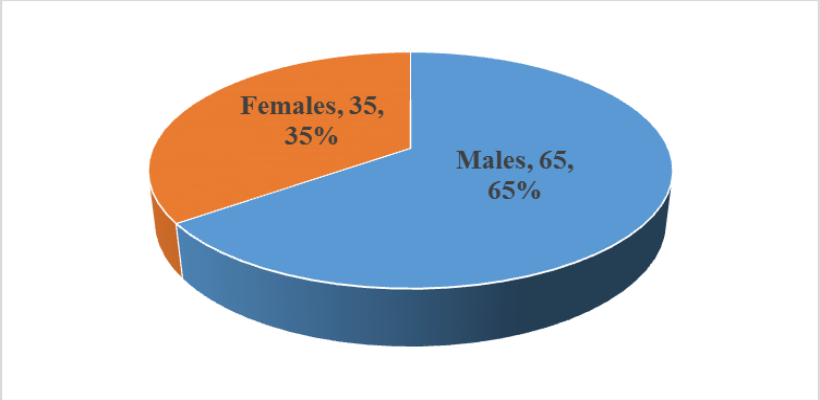

Figure 1: Gender distribution of the studied sample.

Table 1: Age distribution (in years) of the studied sample.

Age in years	Range	Mean ± Standard Deviation (SD)	P value
Males (N=65)	30-80	53.4 ± 10.8	
Females (N=35)	33-70	53 ± 11.1	0.78*
Total (N=100)	30-80	53.6 ± 10.8	

* The difference in mean age (in years) between males and females was statistically not significant (Student's T Test, Df= 98, P=0.78)

More than half of the tumors (52.0%) were found in the right kidney (more among females 57.1%), and radical nephrectomy was performed in 88.0% of the cases (more among males 90.8%) (Table 2). Regarding tumors' site the commonest were in the lower pole (35.0%), followed by the upper pole (26.0%) and the least was found in the middle pole (17.0%). As for tumor type only three types were found in the studied patients; more than three quarters (76.0%) were Conventional renal cell CA/clear cell type, followed by Papillary renal cell CA-type1 (10.0%), Renal cell CA/chromophobe type in 9.0% and Papillary renal cell CA-type2 in 5.0% and in 96.0% of the cases the tumors were unifocal. (Table 3).

Table 2; Distribution of the studied sample by affected kidney and performed surgical operation.

Variable	Males		Females		Total	
	No.	%	No.	%	No.	%
Kidney						
Right	32	49.2	20	57.1	52	52.0
Left	33	50.8	15	42.9	48	48.0
Surgery Performed						
Radical Nephrectomy	59	90.8	29	82.9	88	88.0
Partial nephrectomy	6	9.2	6	17.1	12	12.0

Table 3; Distribution of the patients by tumor's site, type and focalty.

Variable	Males		Females		Total	
	No.	%	No.	%	No.	%
Site						
Upper pole	18	27.7	8	22.9	26	26.0
Middle pole	11	16.9	6	17.1	17	17.0
Lower pole	23	35.4	12	34.3	35	35.0
Extends beyond one pole	13	20.0	9	25.7	22	22.0
Type						
Conventional renal cell CA/clear cell type	47	72.3	29	82.9	76	76.0
Papillary renal cell CA-type1	8	12.3	2	5.7	10	10.0
Papillary renal cell CA-type2	4	6.2	1	2.9	5	5.0
Renal cell CA/chromophobe type	6	9.2	3	8.6	9	9.0
Focality						
Unifocal	62	95.4	34	97.1	96	96.0
Multifocal	3	4.6	1	2.9	4	4.0

Regarding differentiation; Sarcomatoid features were found in 8 patients, three males and five females, in 82.0% were unidentified. As for Microscopical Extension; It was found that the tumor was limited to the kidney in 38 patients (41.6 % in males and 31.4% in females) and was infiltrating perinephric fat in 29 patients (33.9 % in males and 20.0% in females). Regarding grading it was found that nearly half of the patients was G2 (49.0%), followed by G3 (24.0%) and the least was with G1 (6.0%). Pathological staging revealed that the highest proportion of patients were within pT3 (62.0%); 38 males and 24 females, followed by (pT1 31.0%); 22 males and 9 females (Table 4).

Table 4; Distribution of patients by microscopical differentiation.

Variable	Males		Females		Total	
	No.	%	No.	%	No.	%
Differentiation						
Sarcomatoid	3	4.6	5	14.3	8	8.0
Rhabdoid	2	3.1	4	11.4	6	6.0
Both	3	4.6	1	2.9	4	4.0
Unidentified	57	87.7	25	71.4	82	82.0
Microscopical Extension						
Limited to kidney	27	41.6	11	31.4	38	38.0
Infiltrating renal sinus & perinephric fat	8	12.3	9	25.7	17	17.0
Extending to renal pelvis	6	9.2	8	22.9	14	14.0
Infiltrating perinephric fat	22	33.9	7	20.0	29	29.0
Extending to adrenal gland	1	1.5	0	0.0	1	1.0
Extend beyond renal capsule not reaching per-nephric fat	1	1.5		0.0	1	1.0
Grade (NA in 9;6 males & 3 females)						
G1	4	6.8	2	6.2	6	6.0
G2	33	55.9	16	50.0	49	49.0
G3	17	28.8	7	21.9	24	24.0
G4	5	8.5	7	21.9	12	12.0
Pathological Staging						
pT1	22	33.8	9	25.7	31	31.0
pT2	5	7.7	2	5.7	7	7.0
pT3	38	58.5	24	68.6	62	62.0

The size of tumor ranges from 1.5-20 cm with a mean of 6.7 ± 3.3 cm SD, in males it ranges from 2.5-20 cm with a mean of 6.9 ± 3.4 cm SD whereas it ranges in females from 1.5-12 cm with a mean of 6.5 ± 3 cm SD, yet the differences in mean tumor size between males and females was statistically not significant (Student's T Test, Df= 98, P=0.6) (Table 5).

Table 5; Distribution of the studied sample by tumor's size.

Variable	Males	Females	Total	P value
Size (in cm)				
Range	2.5-20	1.5-12	1.5-20	0.6*
Mean ± SD	6.9 ± 3.4	6.5 ± 3	6.7 ± 3.3	

* The difference in mean tumor size (in cm) between males and females was statistically not significant (Student's T Test, Df= 98, P=0.6)

Regarding lympho-vascular invasion; the current study revealed that lympho-vascular invasion was not identified in 91 patients (93.8% of the males and 85.7% of the females) (Table 6) this is on one hand, on the other hand we found that the surgical margins were free in all cases.

Table 6; Distribution of patients by Lympho-vascular invasion.

Lympho-vascular invasion	Males		Females		Total	
	No.	%	No.	%	No.	%
Not identified	61	93.8	30	85.7	91	91.0
Identified	4	6.2	5	14.3	9	9.0

Comparing mean tumor size (in cms) with different pathological stages; it was found that larger tumors were found in patients with pT2 and pT3 compared to pT1 and the differences in mean size were statistically significant (ANOVA, P<0.001) (Table 7) and post Hoc test, Bonferroni, showed that there were statistically significant differences in mean tumor size between patients in stage pT1 and pT2 (P=0.001) and between pT1 and pT3 (P < 0.001)

Table 7; Differences in mean size of tumor and pathological staging.

Pathological Staging	N	Tumor size (in cm) Mean ± SD	95% Confidence Interval for Mean		P value
			Lower Bound	Upper Bound	
pT1	31	3.9 ±1.17	3.484	4.342	<0.001*
pT2	7	8.2 ± 1.2	7.086	9.342	
pT3	62	7.98 ± 3.3	7.157	8.811	
Total	100	6.738	6.090	7.386	

* Statistically significant differences (ANOVA; P<0.001)

Tumor size (in cms) was found to be increasing with advanced staging except for G4 and the differences in mean size was statistically significant (ANOVA, P< 0.001) (Table 8) and post Hoc test, Bonferroni, showed that there were statistically significant differences in mean tumor size between patients in G3 with both G1 (P=0.015) and G2 (P=0.028).

Table 8; Differences in mean size of tumor and grading.

Grade	N	Tumor size (in cm) Mean ± SD	95% Confidence Interval for Mean		P value
			Lower Bound	Upper Bound	
G1	6	3.9 ±1.69	2.148	5.686	<0.001*
G2	49	5.97 ± 2.5	5.244	6.698	
G3	24	8.1 ± 3.9	6.451	9.774	
G4	12	7.7 ± 2.7	6.029	9.471	
Total	91	6.6 ± 3.1	5.98	7.291	

* Statistically significant differences (ANOVA; P<0.001)

Table 9 showed that the association between grading and pathological staging was statistically significant (Fisher's Exact; P< 0.001)

Table 9; Cross tabulation between grading and pathological staging.

Variables	pT1 No. (%)	pT2 No. (%)	pT 3 No. (%)	Total No. (%)	P Value
G1; No. (%)	5 (83.3)	0 (0.0)	1 (16.7)	6 (6.6)	<0.001*
G2; No. (%)	22 (44.9)	4 (8.2)	23 (46.9)	49 (53.8)	
G3; No. (%)	1(4.2)	2 (8.3)	21 (36.8)	24 (26.4)	
G4; No. (%)	0 (0.0)	0 (0.0)	12 (100.0)	12 (13.2)	
Total; No. (%)	28 (30.8)	6 (6.6)	57 (62.6)	91(100.0)	

* Association was statistically significant (Fisher's Exact; P< 0.001)

Table 10 showed that the differences in mean age in years was statistically not significant with grade of tumors (ANOVA, P> 0.05)

Table 11 showed that the differences in mean age in years was statistically not significant with pathological staging of tumors (ANOVA, P> 0.05).

Table 10; Differences in mean age of patients and grading.

Grade	N	Tumor size (in cm) Mean ± SD	95% Confidence Interval for Mean		P value
			Lower Bound	Upper Bound	
G1	6	60.8 ± 6.5	54.05	67.62	0.38*
G2	49	53.5 ± 12.0	50.0	56.9	
G3	24	54.3 ± 7.7	51.08	57.59	
G4	12	51.6 ± 11.9	44.17	59.33	
Total	91	53.9 ± 10.8	51.71	56.18	

*The differences were statistically not significant;(ANOVA; P> 0.05)

Table 11; Differences in mean age of patients and pathological staging.

Pathological staging	N	Mean age in years	95% Confidence Interval for Mean		P value
			Lower Bound	Upper Bound	
pT1	31	54.06 ± 12.1	49.62	58.50	0.59*
pT2	7	49.43 ± 8.0	42.01	56.84	
pT3	62	53.53 ± 10.5	50.86	56.20	
Total	100	53.41± 10.9	51.26	55.56	

*The differences were statistically not significant;(ANOVA; P> 0.05)

DISCUSSION

The incidence of RCC varies internationally ranging from 22 per 100,000 in Czech men to <1 per 100,000 in African countries and is increasing in most countries for both genders.[11] RCC affects men and women in the fifth and sixth decade of life. In the current study nearly two thirds of the patients were males. Patients with RCC were more likely to be male; Hama TH, et al, 2022, from Sulaimaniyah Government, Iraq found 61.5% of their patients with RCC were males.[12] Mahasin SZ et al, 2018, from Saudi Arabia reported that 55% of their patients were males.[11] and. Same results were obtained from other studies.[13 – 16] Regarding age, we found that younger age groups were affected with RCC as their age ranged from 30-80 years with a mean of 53.6 ± 10.8 years SD. Nearly same results was obtained by other studies.[11,12,17] The majority of patients in the current study underwent radical nephrectomy, same result was obtained from Sulaimaniyah-Iraq.[12] unlike other studies were most underwent partial nephrectomy (nephron‑sparing surgery). Partial nephrectomy is the standard of care in the T1a stage. Radical nephrectomy is preferred in the more advanced stages and if possible to be done laparoscopically.[18] Although there are many histological subtypes of RCC, only three types were found in the current study; 76.0% were Conventional renal cell CA/clear cell type, 10.0% Papillary renal cell CA-type1, 9.0% Renal cell CA/chromophobe and 5.0% Papillary renal cell CA-type 2. Globally 90% of RCCs are of the clear cell, papillary and chromophobe histological subtypes, with the clear cell being the most common and aggressive. These subtypes have significant prognostic and treatment-predictive value. Clear cell RCC, which accounts for 75% of diagnoses, is a tumor of renal stem cells commonly in the proximal nephron and tubular epithelium and is most likely to hematogenously metastasize to the lungs, liver and bones.[19,20] Nearly half the cases in the current study were with G2 (The World Health Organization/ International Society of Urological Pathology grading system for clear cell and papillary renal cell carcinoma).[10] and in 62.0% of the patients the pathological staging were with pT3 (According to the College of American Pathologists (CAP) protocol). Most RCC cases in the developed world are found incidentally on imaging, only 10% of patients present with the "classic triad" of symptoms: hematuria, flank pain and palpable masses which may result in diagnosing the tumors with advanced grading and pathological staging.[21] The current study revealed that the size of tumors was significantly larger with advanced pathological staging and grading. A large retrospective study of seven Latin American countries and Spain found that tumor size (> 7 cm) was significantly associated with worsened survival.[21,22] The worse outcome is associated with presence of lympho‑vascular invasion.[11] fortunately lympho-vascular invasion was found only in 9% of the cases.

CONCLUSION

A higher percentage of tumours were Stage pT3 and Fuhrman Grade 2; the male to female ratio was nearly 2:1; the most common type was Conventional renal cell CA/clear cell type; in the majority of cases, the tumour was unifocal; sarcomatoid differentiation was found in only 8% of cases; and in 38% of patients, the tumour was confined to the kidneys.

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