

Clinicopathologic Patterns of Adult Renal Tumors

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ABSTRACT

Background and Aim: Adult renal tumors (ARTs) are rare as compared with tumors of other organs and systems; however, it is important to have demographic and pathology data of rare tumors, including ART. No such data are available from the Kingdom of Saudi Arabia (KSA). Therefore, we aimed to study the demographic and pathological data of ART from King Fahad Hospital, Al-Madinah, KSA.

Materials and Methods: This is a retrospective study of computerized data from the histopathology laboratory of King Fahad Hospital during a 10-year period (January 2006–September 2015).

Results: There were 42 cases of ART, comprising 28 males and 14 females (male:female ratio of 2:1). The study group ranged in age from 17 to 83 years, with a mean of 54.5 years. In the study cohort, 93% of the patients had malignant tumors and 7% had benign lesions. Renal cell carcinoma (RCC) accounted for 85.8% of cases, followed by squamous cell carcinoma and sarcoma. The benign tumors recorded in our series were oncocytoma (4.7%) and angiomyolipoma (2.4%). The tumor size of RCC ranged from 4 to 17 cm, with a mean of 7.4 cm. The majority of patients (68%) had Fuhrman Grade II tumor. Gross capsular invasion, renal vein invasion and lymph node metastases were present in one case each.

Conclusion: We conclude that the pathological findings of ART from the Madinah region are in concordance with studies in national and international literature.

Key words: Adult renal tumors, Al-Madinah, pathology, retrospective

INTRODUCTION

Tumors, especially cancerous tumors, are one of the major health concerns worldwide. According to the 2013 Globocan report, the incidence and prevalence of cancers worldwide were 14.1 million and 32.6 million, respectively; almost half are prevalent in less developed regions.^[1,2] A total of 1,658,370 new cancer cases and 589,430 deaths due to cancer were estimated to have occurred in the United States in 2015.^[3] In the European Union, in 2012, there were approximately 84,000 cases

of renal cell cancer and 35,000 deaths due to kidney cancer.^[4] Renal cell cancers are increasingly being diagnosed worldwide in both men and women.^[5] Rates are generally high in Europe and North America and low in Asia and South America.^[6]

In the Kingdom of Saudi Arabia (KSA), in 2010, there were 284 new diagnosed cases of kidney cancer, accounting for 2.8% of all newly diagnosed cases. This cancer was the 10th most common type of cancer among

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the male population and 12th among the female population. The male to female (male:female) ratio is approximately 1.5:1, as per the Saudi Cancer Incidence Report published in 2014.^[7] Although the Madinah region appears to have a very low incidence of kidney tumors, ranking 10th of the 13 regions in KSA,^[7] there is no other population-based or hospital-based study to highlight the demographic and pathological data of adult renal tumors (ARTs) in Madinah. In this study, we aimed to study the demographic and pathological data available at King Fahad Hospital, Al-Madinah, which would be the first of its kind in this region, to help clinicians and relevant authorities in the region in the diagnosis and planning of management strategies of ART.

MATERIALS AND METHODS

This was a retrospective study of ARTs diagnosed in the Department of Pathology of King Fahad Hospital, Al-Madinah, KSA, between January 2006 and September 2015. The frequency of all ARTs was collected from the pathology reports and was divided into two groups, i.e., benign and malignant groups. Detailed histopathologic characteristics including side of involvement, tumor type (according to WHO classification), tumor size, tumor grade, lymph node status, capsular invasion and renal vein invasion were assessed for the malignant ART group and analyzed using the SPSS version 19 software (SPSS Inc., Chicago, IL, USA). Fuhrman's nuclear grade system was applied to all 36 cases of renal cell carcinoma (RCC). Inclusion criteria were total, radical or partial nephrectomies performed for benign and malignant tumors of adult patients (≥ 17 years of age). Nephrectomies performed for nonneoplastic conditions and cases of ART whose blocks or slides could not be retrieved were excluded from the study.

The hematoxylin and eosin slides were reviewed to confirm the histopathological diagnosis. No immunohistochemistry was performed as the diagnoses were made before the introduction of the immunohistochemistry technique in the Department of Pathology at the King Fahad Hospital.

As this was a retrospective study predominantly involving computer data analysis and retrieval of archived blocks and slides, this study was exempted from ethical approval.

RESULTS

During the study period, 42 cases of ARTs were identified, of which 28 (66.7%) patients were males and 14 (33.3%) patients were females, with a male:female ratio of 2:1.

The age of the patients ranged from 17 to 83 years, with a mean age of 54.5 years.

The majority of the cases ($n = 20$; 47.6%) were seen in the age group 50–69 years. The young age group (≤ 40 years) and the elderly age group (≥ 70 years) constituted 19% and 21.4%, respectively. The left kidney was involved in 27 cases (64.3%), while the right kidney was involved in 15 cases (35.7%). Based on the pathological assessment of the patients undergoing surgical treatment with the preoperative diagnosis of renal tumor, 39 cases (93%) had malignant tumors and 3 cases (7%) had benign lesions.

The histological type and frequency of distribution of patients with renal tumors are shown in Table 1. RCC constituted the major proportion of renal tumors, occurring in 85.8% of cases. Of these, 69.5% cases were conventional/clear cell RCC, 16.7% chromophobe RCC, 11.1% papillary RCC and 2.7% collecting duct RCC. Other malignant tumors included were squamous cell carcinoma (SCC) (4.7%) and high-grade pleomorphic undifferentiated sarcoma (2.4%). Benign renal tumors recorded in our series were oncocytoma (4.7%) and angiomyolipoma (2.4%) [Table 1].

The main clinicopathological characteristics of RCC are given in Table 2, which shows that of the 36 RCC patients, 24 were males (66.7%) and 12 (33.3%) were females. The male:female ratio was 2:1. The mean age at diagnosis was 54.2 years. The majority of the cases ($n = 17$; 47.3%) were seen in the 50–69 years age group. Both the young age group (≤ 40 years) and the elderly age group (≥ 70 years) constituted 19.4% [Table 2]. Almost a similar pattern of age group distribution was seen in all subtypes of RCC. The tumor size ranged from 4 to 17 cm, with a mean size of 7.4 cm. The mean size of tumor in conventional/clear cell RCC, chromophobe RCC and papillary RCC subtypes were 7.1, 7 and 8.5 cm, respectively [Table 2].

Table 1: The histological type and frequency of distribution of our patients with renal tumors

Histopathologic diagnosis	Frequency (%)
Malignant tumors	
Renal cell carcinoma	36 (85.8)
Squamous cell carcinoma	2 (4.7)
Sarcoma	1 (2.4)
Benign tumors	
Oncocytoma	2 (4.7)
Angiomyolipoma	1 (2.4)
Total	42 (100)

Table 2: The clinicopathological features of renal cell carcinoma subtypes					
Variable	All cases	Clear cell RCC	Chromophobe RCC	Papillary RCC	Collecting duct RCC
Gender, n (%)					
Male	24 (66.7)	15 (60)	5 (83.3)	3 (75)	1 (100)
Female	12 (33.3)	10 (40)	1 (16.7)	1 (25)	-
Age					
Mean age ± SD (years)	54.2 ± 13.5	52.5 ± 13.1	50.8 ± 12.7	53.7 ± 13.4	60 ± 15
Age-specific groups, n (%)					
<40	7 (19.4)	4 (16)	2 (33.3)	1 (25)	-
40–49	5 (13.9)	5 (20)	-	-	-
50–59	11 (30.6)	8 (32)	2 (33.3)	1 (25)	-
60–69	6 (16.7)	3 (12)	2 (33.3)	-	1 (100)
≥70	7 (19.4)	5 (20)	-	2 (50)	-
Tumor size					
Mean size ± SD (cm)	7.4 ± 2.5	7.1 ± 2.4	7 ± 2.3	8.5 ± 2.8	7.3 ± 2.4
Size-specific groups, n (%)					
<5	15 (41.7)	13 (52)	2 (33.3)	-	-
5–10	17 (47.2)	10 (40)	3 (50)	3 (75)	1 (100)
>10	4 (11.1)	2 (8)	1 (16.7)	1 (25)	-
Tumor grade, n (%)					
Grade I	6 (16.7)	4 (16)	-	2 (50)	-
Grade II	22 (61.1)	17 (68)	3 (50)	2 (50)	-
Grade III	8 (22.2)	4 (16)	3 (50)	-	1 (100)

RCC – Renal cell carcinoma; SD – Standard deviation

Fuhrman's nuclear grade system was applied to all 36 cases of RCC. Among 25 cases of conventional/clear cell RCC, 4 (16%) were Grade I, 17 (68%) were Grade II and 4 (16%) were Grade III. Among six cases of chromophobe RCC, three (50%) were Grade II and three (50%) were Grade III. Similarly, two cases of papillary RCC (50%) were Grade I and two cases (50%) showed Grade II histology [Table 2].

Gross capsular invasion with the involvement of perinephric fat was observed in one case. Similarly, renal vein invasion was also found on gross examination in only one case. Lymph nodes were received in four cases. Lymph node metastases were present in one case, with the remaining three nodes showing reactive changes.

Other malignant tumors included were two cases of SCC (4.7%) and a case of high-grade pleomorphic undifferentiated sarcoma (2.4%). For SCCs, the male:female was 1:1 and the mean age was 67.5 years. Both cases were moderately differentiated and both cases were associated with renal stones.

A sarcoma was seen in a 53-year-old male patient. Benign renal tumors recorded in our series were two cases of oncocytoma (4.7%) and one case of

angiomyolipoma (2.4%). Both cases of oncocytoma were in male patients. The mean age at diagnosis was 67 years. The angiomyolipoma was seen in a 17-year-old female.

DISCUSSION

With the overall increase in the prevalence and incidence of most commonly encountered cancers, renal tumors also appear to show an increasing incidence in both males and females.^[5] Although there is sufficient epidemiological data of ART globally and nationally, there was a deficiency of hospital-based pathological studies in the KSA, especially in the Al-Madinah region. We report our hospital-based ART pathology experience in relation to demographical and detailed pathological parameters based on nephrectomies performed in the tertiary care hospital of the region.

In our study, we found renal tumors to be more prevalent in males, with a male:female ratio of 2:1. Although most literature on ART has reported that males are predominantly affected by ART, the male:female ratios vary considerably. The Saudi Cancer Incidence Report published in 2014 has provided a male:female ratio of approximately 1.5:1, which is significantly different from our observation.^[7] However, our findings are in concordance with a recent Australian

study, which reported a male:female incidence ratio of approximately 2:1.^[8] A similar ratio has also been reported by a group in Pakistan and in a study on nephrectomies from south KSA.^[9,10] On the contrary, in 2011, Tayib collected data of 124 ARTs from across KSA and found a high male:female ratio of 3.4:1.^[11] More recently, in studies conducted in Poland and Lebanon for ART, high male:female ratios of 4.7:1 and 4:1, respectively, were found.^[12,13] Therefore, the gender-related observation in our present study is in concordance with all available data in national and international literature. However, there are variations in the degree of male:female ratios, ranging from a minimum of 1.5:1 to a maximum of 4.17:1. These variations are probably attributed to different methodologies applied and the size of samples available to the researchers at that particular time and place.

Regarding the age parameters of ART, our findings are consistent with the Saudi national figures reported in the Cancer Incidence Report in 2014.^[7] These findings are also consistent with some recent individual hospital-based studies from the KSA, Poland and Pakistan.^[11,12,14] Khafaja *et al.* reported a higher median age of 62.4 years in Lebanon,^[15] whereas Latif *et al.* reported a lower mean age of 47.9 years in their preliminary report on ART on a Pakistani population.^[9] Recently, a report from South India found a significantly low mean age of 39.5 years in ART of nephrectomy patients.^[15] Similarly, Siegel *et al.*, in their study from the United States, found that RCC rates are increasing in children and adolescents.^[16] We also observed that almost one-fifth (19%) patients of ART were aged <40 years, with the youngest patient being aged 17 years. Thus, our age-related findings are within the range reported in international and national studies, i.e., 54.5 years in a range of 39.5–62.4 years. The trend of increased diagnosis of ART at a younger age was also observed in our study. The differences in the findings of different studies are probably because of different

methodologies applied and geographical populations studied. The findings of some recent relevant studies have been compared with that of the present study in Table 3.

RCC was the most common type of ATR and accounted for >85% cases in our study. The most common subtype of RCC was clear cell type (69.5%). Recent literature depicts a wide variation in the percentage frequency of RCC in different studies. From Pakistan, we can compare two recent studies. Latif *et al.* reported that 87.2% of ARTs were RCC, of which the clear cell type accounted for 73.2%.^[9] Hashmi *et al.* found 78% of ARTs to be RCC, of which the clear cell subtype accounted for 62%.^[14] Reddy *et al.*, in southeastern India, observed 75.2% of ARTs to be RCC, of which the clear cell type accounted for >90%.^[17] In contrast to the above studies, Khafaja *et al.* found 71% of ARTs to be RCC, of which clear cell carcinoma accounted for only 59.1%.^[15] The demographics of a study of 124 cases from the Western region of KSA reveal clear cell RCC in 66 (53.2%) cases, sarcomatoid carcinoma in 10 (8.0%) cases and papillary RCC in 12 (9.67%) cases.^[11] In an earlier study conducted in 1996, Talic and El-Faqih collected data of renal tumors from all over KSA and found 33 patients (76.7%) who had RCC.^[18] Thus, our observation on the type of ART is consistent with the national and international literature. The male:female ratio (i.e., 2:1) remained the same for RCC as it was for total ART tumors. In recent literature regarding the RCC gender incidence, a Malaysian study observed the same male:female ratio of 2:1.^[19] An almost similar male:female ratio (1.9:1) was found by a group reporting from a southern city of Pakistan,^[14] whereas another study from a northern region of Pakistan reported a slightly lower male:female ratio of 1.5:1.^[20] Geographically close to the KSA, in Lebanon, Khafaja *et al.* reported a significantly high male:female ratio of approximately 3.5:1.^[15] Completely opposing figures have been reported by a Nigerian group from Ibadan,

Table 3: Comparison of basic adult renal tumors data with regional studies

Regional studies	Year	Country	Number of patients	Male:female ratio	Mean age	Age range	Percent of RCC cases
Talic <i>et al.</i>	1996	Riyadh, KSA	43	1.3:1	50.9	N/A	76.6
Latif <i>et al.</i>	2011	Pakistan	50	2:1	47.9	17–80 years	87.2
Tayib	2011	Jeddah, KSA	124	3.4:1	54.08	27–86 years	53.2
Reddy <i>et al.</i>	2012	India	113	1.7:1	N/A	1 month to >70 years	90.5
Yap <i>et al.</i>	2013	Malaysia	151	2:1	60.7	34–83 years	87.6
Hashmi <i>et al.</i>	2014	Pakistan	68	2:1	56.4	18–84 years	78
Present study (Albasri <i>et al.</i>)	2016	Al-Madinah, KSA	42	2:1	54.5	17–83 years	85.5

N/A – Not available; RCC – Renal cell carcinoma

who reported a male:female ratio of 1:1.^[21] From within the KSA, there is only one comparable study by Talic and El-Faqih, who reported a male:female ratio of 1.3:1.^[18]

In our experience, the mean age of RCC diagnosis in our patient cohort is 54.2 years. This is in keeping with the observation of Ghosn *et al.*, who found that the age of diagnosis (mean <60 years) in North Africa and the Middle East is lower than in Western countries.^[22] All available reports from recent literature are consistent with these observations. The mean age of RCC diagnosis has been reported to be as low as 48 years in Nigeria and to as high as 60 years in Malaysia and 60.3 years in Lebanon.^[13,19,21] In 1996, a significantly low mean age of RCC diagnosis (50.9 years) was reported in the KSA.^[18]

Regarding the tumor size of RCC in our patients, we could only find four studies in recent literature for comparison. We found a mean tumor size of 7.4 cm. Only one study from the south of Pakistan found an RCC tumor to be 7.2 cm in size, which is slightly lesser than our finding.^[14] However, there are two more studies from north and south of Pakistan that both reported a mean tumor size of >8 cm.^[9,20] A study conducted in India reported a mean RCC size of 8.08 cm. Furthermore, this report also noted that a tumor size of <4 cm was present in only 10.4% of patients.^[23] In our study, most tumors were categorized as Fuhrman's Grade II (68%) and 16% each were categorized as Grade I and III; there were no Grade IV cases. Similarly, Latif *et al.* also reported that most cases were identified as Grade II (63.3%), followed by Grade III tumors (20%).^[9] In another study conducted on the same population, Hashmi *et al.* reported that most RCCs were intermediate to high grade (60% and 40%, respectively).^[14] Features of aggressive higher stage tumors, such as gross capsular invasion, renal vein invasion and lymph node involvement was observed in occasional cases. Latif *et al.* found gross capsular invasion in 14 cases (34.1%) and gross renal vein invasion in 7 cases (17%) and commented that most of their cases (68.2%) presented at advanced stages.^[9] Our observations regarding the pathological data of RCC are concordant with literature; however, only a few recent studies were available for comparison.

We found two cases of benign tumors (one case of oncocytoma and one case of angiomyolipoma) and two cases of malignant tumors (one case of SCC and one case of undifferentiated sarcoma). Because of the rarity of these tumors, it would be irrelevant to present a detailed comparison of these tumors with those observed in recent

literature. However, the frequency of these rare tumors is comparable with other reports from Pakistan and India.^[9,14,15] On the contrary, a 1996 study from the KSA observed a higher percentage of angiomyolipoma.^[18] This could probably be because of geographical variation or a possible increase in the diagnosis of RCC after two decades, leading to an apparent decrease in the frequency of benign tumors.

CONCLUSION

This study demonstrated that the demographic and pathological findings of ART in the Al-Madinah region are consistent with national and international figures. However, ART appears to affect the younger individuals in our population. This difference may be due to geographical and/or racial variation or possibly due to the small sample size in our study. Further pathology-based studies of larger patient cohorts at regional and national levels are recommended.

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Conflicts of interest

There are no conflicts of interest.

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