Original Article

Comparative analysis of histopathological subtypes of renal cell carcinoma in the Middle East compared to other world regions

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Abstract

Introduction: Renal cell carcinoma (RCC) has various histopathological tumor subtypes which have a significant implication on the oncological outcome of these patients. We aimed to evaluate the distribution of RCC subtypes presenting at a tertiary care center in the Middle East, in comparison to the distribution reported in different geographic areas worldwide.

Methods: A retrospective chart review was conducted on all patients who underwent partial or radical nephrectomy for RCC at the American University of Beirut Medical Center between January 2012 and January 2018. Data on histologic subtypes were compiled and compared to representative series from different continents.

Results: One hundred and seventy-nine patients with RCC were identified, of whom 122 (68.2%) were classified as clear cell, 30 (16.8%) as papillary, 17 (9.5%) as chromophobe, and 10 (5.6%) as unclassified. When compared to other regions of the world, this Middle Eastern series demonstrated a higher prevalence of the chromophobe subtype compared to Western populations (9.5% in the Middle East vs. 5.3% in the US and 3.1% in Europe) and a lower prevalence of clear cell subtype (68.2% in the Middle East vs. 78.7% in the US and 85.8% in Europe). Conversely, there was a higher prevalence of papillary RCC in the Middle East (16.8%) compared to North America (13.1%, 95% confidence interval [CI]: 12.7–13.6), Europe (11.1%, 95% CI: 10.0–12.1), and Australia (10.2%). The prevalence of chromophobe and clear cell RCC in the Middle East was similar to that reported in South America.

Conclusions: The distribution of RCC subtypes in this Middle Eastern cohort was significantly different from that reported in the Western hemisphere (Europe and the US) but similar to that reported in South America and Australia. These findings may point to a possible genetic predisposition underlying the global variation in distribution.

Keywords: Chromophobe renal cell carcinoma, histopathological subtypes of renal cell carcinoma, Middle East

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INTRODUCTION

There has been a progressive rise in the incidence of renal cell carcinoma (RCC) in the Western hemisphere, attributed mainly to the wide adoption of cross-sectional imaging and increased detection of asymptomatic lesions.[1] Several risk factors for RCC have been identified and include cigarette smoking, obesity, and hypertension. The most commonly encountered histopathological types are clear, papillary, and chromophobe subtypes of renal parenchymal cancers, based on the Heidelberg classification system.[2] The histopathological subtypes of RCC vary based on genetic, molecular, and geographic considerations.[3] Several studies have suggested that histopathological subtypes of RCC have a significant impact on the oncologic outcome of afflicted patients.[4] However, there are limited data on the prevalence of RCC and its pathological subtypes in the Middle East. We sought to evaluate the distribution of subtypes of RCC at presentation in a tertiary health-care center in Lebanon, the American University of Beirut Medical Center (AUBMC). This referral center provides advanced oncological care to patients from several neighboring states, thus providing a sample of the population in this region. In order to explore for any similarities and differences in trends, our data were further compared to reports from other geographic districts in the world, obtained by searching the recent literature.

METHODS

After securing institutional Internal Review Board approval, a retrospective chart review of all patients who underwent radical or partial nephrectomy for solid renal masses between January 1, 2012, and January 1, 2018, was performed. Data were obtained from chart reviews and electronic records, noting patient demographics, predisposing factors, preoperative tumor characteristics, and complexity, with special attention to the evaluation of the histological subtypes of RCC.

Four subtypes of RCC were documented: clear cell, papillary, chromophobe, and unclassified. For the clear cell subtype, the cancerous cells had a clear cytoplasm with a distinct membrane surrounding the cells, irrespective of cytoarchitecture (acinar or alveolar). Papillary renal cell carcinoma (papRCC) cells were cuboidal/columnar with an eosinophilic cytoplasm. Chromophobe renal cell carcinoma (ChrRCC) subtype cells had pale cytoplasm that was slightly positive for periodic acid–Schiff and strongly positive for colloid stain (Hale's acid iron).[5,6]

Data on the reported frequency of histological subtypes of RCC from various geographic world regions were compiled from several publications, and weighted averages were calculated and compared to the Middle Eastern population. Descriptive statistics were performed and tabulated and histogram figures were made for comparison purposes.

RESULTS

One hundred and seventy-nine cases of RCC were identified. Table 1 depicts the demographic characteristics. One hundred and thirty-five (75.4%) were male and 44 (24.6%) were female. The mean age (years) was similar among states in the region except for Syrian patients who were relatively younger (48 years) than Lebanese, Iraqis, and others (58 years). The percentage of smokers was similar in Lebanese and Syrian patients (47–57%), and both were appreciably higher (almost double) than that reported in the Iraqi patients (27.5%).

Table 2 depicts the patient characteristics and demographics based on RCC histological subtype and nationality. Of 179 RCC cases, clear cell renal cell carcinoma (ccRCC) was identified in 122 (68.2%), papRCC in 30 (16.8%), ChrRCC in 17 (9.5%), and unclassified RCC in 10 (5.6%). The age was 57 ± 12.8 for the ccRCC, 61 ± 15.1 for papRCC, 55 ± 12.9 for ChrRCC, and 54 ± 22.6 for unclassified RCC. Gender distribution in each subtype was similar and not different from that of other world populations. Smoking exposure was similar among Middle Eastern nationalities except for the Iraqis who had substantially lower exposure.

Table 3 depicts the frequency of RCC histological subtypes in select reports from various geographic areas worldwide, including weighted averages in case of more than one report from the same region. Our findings as compared to those reported in the worldwide literature are summarized as follows: the prevalence of ccRCC in this study (68.2%) was lower than the reported prevalence of ccRCC in all other world regions. Conversely, there was a higher prevalence of papRCC in the Middle East (16.8%) compared to that reported in other regions: North America (13.1%, 95% confidence interval [CI]: 12.7–13.6), Europe (11.1%, 95% CI: 10.0–12.1), Australia (10.2%), and Asia (5.0%, 95% CI: 4.5–5.5). ChrRCC was identified in 9.5% of patients in the Middle East, about double that reported in the US (5.3%, 95% CI: 5.0–5.7), and almost triple of that reported in the European literature (3.1%, 95% CI: 2.5–3.7), and similar to what is reported in the South American (10.3%, 95% CI: 7.7–13.4) and Australian literature (8.2%).

DISCUSSION

The prevalence of RCC subtypes was substantially different in our population than that reported worldwide [Figure 1].

Table 1: Distribution of patients with renal cell carcinoma based on Middle Eastern nationality

	Total RCC	Lebanese	Iraqi	Syrian	Other (Palestine/UAE/KSA/JRD)
Number of patients (%)	179 (100.0)	124 (69.3)	40 (22.3)	7 (3.9)	8 (4.5)
Age range (years)	13-86	13-86	15-81	22-79	53-64
Mean age±SD	58±14.0	58±13.7	57±14.3	48±22.2	58±3.7
Sex (%)					
Male	135 (75.4)	91 (73.4)	33 (82.5)	5 (71.4)	5 (62.5)
Female	44 (24.6)	33 (26.6)	7 (17.5)	2 (28.6)	3 (37.5)
Smokers (%)	76 (42.5)	59 (47.6)	11 (27.5)	4 (57.1)	2 (25.0)

RCC: Renal cell carcinoma, SD: Standard deviation

Table 2: Patient characteristics and demographics based on renal cell carcinoma histological subtype and nationality

	Total RCC cases	RCC histological subtype			
		Clear cell	Papillary	Chromophobe	Unclassified RCC
Number of patients (%)	179 (100.0)	122 (68.2)	30 (16.8)	17 (9.5)	10 (5.6)
Age range - years	13-86	25-86	13-80	31-74	19-84
Mean age±SD	58±14.0	57±12.8	61±15.1	55±12.9	54±22.6
Nationality (%)					
Lebanese	124 (69.3)	85 (68.6)	18 (14.5)	15 (12.1)	6 (4.8)
Iraqi	40 (22.3)	29 (72.5)	8 (20.0)	0 (0.0)	3 (7.5)
Syrian	7 (3.9)	3 (42.8)	2 (28.6)	1 (14.3)	1 (14.3)
Other	8 (4.5)	5 (62.5)	2 (25.0)	1 (12.5)	0 (0.0)
Smokers (%)	76 (42.5)	56 (73.7)	11 (14.5)	6 (7.9)	3 (3.9)

RCC: Renal cell carcinoma, SD: Standard deviation

Table 3: Frequency of renal cell carcinoma histological subtypes in select reports from various geographic areas worldwide

	Cases (*n*)	Clear cell, *n* (%)	Papillary, *n* (%)	Chromophobe, *n* (%)	Unclassified, *n* (%)
USA					
Keegan *et al*. (2012)[7]	17,650	13,841 (78.6)	2278 (12.9)	949 (5.4)	NA
Leibovich *et al*. (2010)[3]	3062	2466 (80.5)	438 (14.3)	158 (5.2)	NA
Weighted average (%) (95% CI)		78.7 (78.2-79.3)	13.1 (12.7-13.6)	5.3 (5.0-5.7)	NA
Europe					
Pichler *et al*. (2012)[8]	2660	2263 (85.1)	309 (11.6)	88 (3.3)	NA
Gudbjartsson *et al*. (2005)[9]	629	558 (88.7)	53 (8.4)	13 (2.1)	NA
Weighted average (%) (95% CI)		85.8 (84.5-87)	11.0 (10.0-12.1)	3.1 (2.5-3.7)	NA
Australia					
Doeuk *et al*. (2010)[10]	483	391 (78.4)	51 (10.2)	41 (8.2)	NA
Asia					
Wu *et al*. (2017)[11]	3479	3084 (88.6)	174 (5.0)	221 (6.4)	NA
Kanayama *et al*. (2015)[12]	3648	2818 (77.2)	182 (5.0)	115 (3.2)	45 (1.2%)
Weighted average (%) (95% CI)		82.8 (81.9-83.7)	5.0 (4.5-5.5)	4.7 (4.2-5.2)	NA
South America					
Ornellas *et al*. (2012)[13]	227	165 (72.7)	24 (10.5)	24 (10.6)	NA
Dall'Oglio *et al*. (2008)[14]	230	148 (64.3)	45 (19.6)	23 (10.0)	NA
Weighted average (%) (95% CI)		68.5 (64-72.7)	15.1 (11.9-18.7)	10.3 (7.7-13.4)	NA
Middle East (present study) Khauli *et al*. (2019)	179	122 (68.2)	30 (16.8)	17 (9.5)	10 (5.6%)

CI: Confidence interval, NA: Not available

In the Middle East, the prevalence of ccRCC was lower, while papRCC and ChrRCC were higher compared to the reported prevalence in North America, Europe, and Australia. Furthermore, the prevalence of RCC subtypes in the Middle Eastern population was similar to those reported in South America (ccRCC: 68.2% and 68.5%, respectively, papRCC: 16.8% and 15.1%, respectively, and ChrRCC: 9.5% vs. 10.3%, respectively). The prevalence of ChrRCC subtype in this study was also similar to that in Australia (9.5% vs. 8.2%, respectively). There was a higher prevalence of the ChrRCC subtype in this study (9.5%) than that reported in North America (5.4%), Europe (3.2%), and Asia (5.3%) [Figure 1]. These findings are consistent with our previous cohort study conducted at AUBMC, wherein 23% of patients were found to have ChrRCC, a significantly larger proportion than that reported elsewhere in the world.[10] In the current study, the prevalence of ChrRCC remains higher than that of the Western hemisphere (almost double), although it is less than what we had reported previously for the RCC population that presented between 2002 and 2012.[14] Similarly, according to a study conducted in King Abdul Aziz in Saudi Arabia, ChrRCC subtype accounts for 13.79% and papillary subtype accounts for 10.84%.[15]

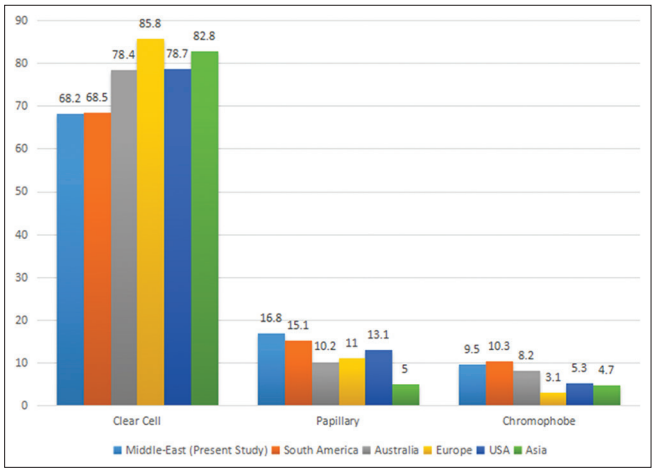

Figure 1: Histogram depicting the distribution of renal cell carcinoma subtypes (prevalence) based on geographic districts worldwide

We hypothesize that there might be an ethnic or perhaps a genetic predisposition accounting for this similarity, which could be due, to a large extent, to a massive wave migration from the Middle East to South America in the early 20th century. Alternatively, other acquired or yet undefined environmental predisposing factors may be implicated in these observation associations.

We acknowledge some deficiencies in this retrospective study that may limit the drawing of any definitive conclusions. Our assumption that the AUBMC represents a tertiary referral center that draws its patients in a balanced fashion from Middle Eastern states may be subject to criticism, as it may not be truly representative of the region's population. Furthermore, comparative evaluations with noncontemporary cohort studies from different regions in the world have its own limitations. Finally, we acknowledge that the surgical sample in itself may not be accurately representative due to possible selection bias since patients with more aggressive tumors and metastatic disease at presentation were not included in this cohort of surgical patients.

CONCLUSIONS

The prevalence of ChrRCC in the Middle Eastern population who underwent surgery is substantially higher compared to the European and North American populations (and similar to that reported in the South American and Australian populations). There was a lower prevalence of ccRCC in the Middle East compared to the European and North American populations. These findings could be attributed to genetic similarity related to population migration from the Middle East or alternatively environmental and dietary factors. Further prospective studies addressing genetic and environmental influences on pathogenesis and outcome of RCC subtypes are warranted.

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Conflicts of interest

There are no conflicts of interest.

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