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ORIGINAL RESEARCH

Epidemiological and Histopathological Characteristics of Renal Cell Carcinoma in Somalia

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Background: There is a scarcity of studies regarding renal cell carcinoma (RCC) reported from Sub-Saharan Africa.

Objective: The present study is the first report evaluating the prevalence and clinical and histopathological features of RCC at a tertiary hospital in Somalia.

Methods: This retrospective study included 84 patients with histologically confirmed RCC over 5-years. The investigated parameters were sociodemographic features, radiological and histopathological characteristics, mortality, and overall 5-year survival rate.

Results: The prevalence of RCC in our study was 0.7%. The mean age of the patients was 53.74±5.5 years, 67.9% were male, and 32.1% were female, with a 2:1 male-to-female ratio. The mean tumor size was 6.38±2.4 cm. Clear cell RCC was the most common histological type in 67.8%, followed by papillary RCC (15.6%), unclassified RCC (9.5%), and chromophobe RCC was the least common in 7.1% of the cases. About one-third of the case had locally advanced RCC with positive nodal involvement, 26.2% of the patients had metastatic disease, and a further 6% progressed to metastatic cancer despite surgical resection. Eight percent of our cases returned with local recurrence. The mortality rate was 37.2%. More than eighty percent of females had a low-stage and a low-grade RCC, while males held higher stages and higher grades RCC in 37% and 63%, respectively ($p<0.001$). Smokers were male-only, while obesity was common in female patients ($p=0.02$).

Conclusion: The study findings showed a satisfactory outcome, 71.4% of our patients presented with localized RCC, the five-year survival rate of the patients was 62.8%, and the mortality rate was substantially higher for patients with a higher stage, a higher grade tumor, and metastatic disease at the time of diagnosis.

Keywords: renal cell carcinoma, Sub-Saharan Africa, mortality, five-year survival rate

Introduction

Renal cell carcinoma (RCC) is a molecularly and histopathologically group of heterogeneous tumors. The most common subtypes of RCC are Clear cell RCC (65–70%), papillary RCC (15–20%), and chromophobe RCC (5–7%), respectively.[1]

The prevalence of renal cell carcinomas (RCCs) represents 3% of all visceral neoplasms and is the seventh most common cancer with an increasing prevalence.[2] RCC accounts for 90% of tumors originating from the kidneys. It is common in the sixth and seventh decade of life with a median age of 64 years and primarily is a disease of the elderly, with a twofold male predominance.[3,4]

Smoking, male gender, age, hypertension, and obesity are several risk factors related to RCC.[5,6] A first-degree relative is also associated with an increased risk of having RCC.[7]

The severity and prognosis of RCC correlate with the tumor stage, histopathological grade, presence of sarcomatoid and rhabdoid features, and fat and vascular invasion.[8]

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Despite the advancements in diagnosis and management of RCC in the last two decades, RCC still is the most lethal urological cancer resulting in a mortality rate of about 40%.[2] In recent years, RCC incidence increasing worldwide and per nation, despite the majority of the renal tumors being identified accidentally through medical imaging (abdominal ultrasound and computed tomography).[9] In cases of metastatic tumors, the mortality of RCC is high, with a low survival rate of about 0–13%.[10]

Cancer is one of the leading causes of mortality worldwide. Before the age of 70, cancer is the first or second cause of death in 91/172 countries and the third or fourth cause of death in twenty-two countries.[11] Africa has the lowest RCC incidence and mortality rate, with a cumulative risk below 0.2% for both gender groups. Egypt (2.4), Libya (2.3), Mali (1.8), and Tunisia (1.7) had the highest mortality rates, with a cumulative mortality risk between 0.17% and 0.27%.[12]

The present study is the first report from Somalia evaluating the prevalence and clinical and histopathological features of RCC at a tertiary hospital (the sole tertiary and referral hospital and the only cancer center) in Somalia.

Method

This retrospective study included all patients who have received the diagnostic code of RCC in agreement with the International Classification of Diseases (ICD-10) system and underwent contrast-enhanced computed tomography of the abdomen and nephrectomy over 5-years using the electronic hospital information system (HIS). The study included 84 patients with histologically confirmed renal cell carcinoma. Patients with the Bosniak classification system indicating benign renal cyst, those with inflammatory and metastatic mass with known other primary origins, and patients with incomplete data were excluded from the study.

Investigated parameters of the patients included age of the patients, gender group, site of the tumor (right, left, and bilateral), location of the mass (upper pole, middle pole, lower pole, and more than one pole of the kidney), clinical tumor stage, lymph node involvement, distant metastasis, and type of operation (laparoscopic, open vs radical, partial nephrectomy). Axial (with 1 mm cross-section), coronal and sagittal planes of CT abdominopelvic with and without contrast were used to determine renal mass size and localization. Histopathological results such as type of renal cell carcinoma, grade of the tumor in accordance to the World Health Organization/International Society of Urologic Pathology

(WHO/ISUP) grading systems were evaluated too.

WHO/ISUP grading system 2016, fourth edition, is the current internationally recommended system for typing renal tumors and was used to report the histopathological findings. T stage was classified into pTX: primary tumor cannot be assessed, pT0: No evidence of primary tumor, pT1a: $\leq$ 4 cm, limited to the kidney, pT1b: > 4 cm and $\leq$ 7 cm, limited to the kidney, pT2a: > 7 cm and $\leq$ 10 cm, limited to the kidney, pT2b: > 10 cm, limited to the kidney, pT3a: invades renal vein/branches, perirenal fat, renal sinus fat or pelvicalyceal system, pT3b: extends into vena cava below the diaphragm, pT3c: extends into vena cava above the diaphragm or invades vena cava wall, pT4: invades beyond Gerota fascia, including a direct extension to the adrenal gland.

WHO/ISUP grading system: Grade 1: Nucleoli are absent or inconspicuous and basophilic at 40x. Grade 2: Nucleoli are not prominent at 10x but visible and eosinophilic at 40x. Grade 3: Nucleoli conspicuous and eosinophilic at 10x. Grade 4: Extreme nuclear pleomorphism, multinucleated cells, and rhabdoid or sarcomatoid differentiation.

The ethical research board committee of Mogadishu Somalia Turkish Training and Research Hospital (REF. MSTH-9006) approved the research. In addition, all study participants and a parent of participants under 18 years of age previously consented to use their medical and surgical data in this study. This study was carried out in accordance to the Helsinki Declaration contents.

Statistical analyses were used in the Statistical Package for Social Sciences (SPSS-IBM) for Windows version 23. The data were analyzed using univariate descriptive statistics. The frequencies and percentages, as well as the mean ± (SD), were presented. Cross-tabulations were used to determine the association between the variables.

Results

A total of 84 patients with histopathologically proven RCC over 5-years were included in this study. The prevalence of RCC in our study was 0.7%. The mean age of the patients in our study was 53.74±5.5 years, 48.8% of the cases were

elder (≥60 years), and 38.21% were between 40–59 years, while 13% of the patients were younger than 40 years. The gender distribution of RCC was 67.9% male and 32.1% female, showing more than twofold male predominance. The mean tumor size was 6.38±2.4 cm. The right kidney harbored most of the masses in 57%, 40.5% in the left, while 2.4% were bilateral involvement (Table 1). Open radical nephrectomy was the predominant operation performed in 54.7% of the cases, 32% underwent laparoscopic radical nephrectomy, and the remaining 13% underwent open partial nephrectomy. As shown in Table 2, Clear cell RCC was the most common histological type in about 67.8%, followed by papillary RCC (15.6%), unclassified RCC (9.5%), and Chromophobe RCC was the least common in 7.1% of the cases. Half of the patients held tumor stage 2, followed by T1 in 21.4%, 15.5% in T4, and 13.1% in T3. WHO/ISUP grading system revealed that half of the patients had high-grade tumors (G4 in 28.7% and G3 in 20.2%), while the remaining 50% had low-grade tumors (G2 in 44% and G1 in 7.1%). Three cases had rhabdoid features, two male and one female patient. About one-third of the case had locally advanced RCC with positive nodal involvement, while 26.2% of the cases revealed distant metastasis such as lungs. Regarding the comorbidities, 28.6% had diabetes, 25% were obese, 19% of the patients had hypertension, and 15.4% were smokers. One patient with a left upper pole 7cm mass who had undergone laparoscopic radical nephrectomy developed a pancreatic tail injury, which transformed into necrotizing pancreatitis. Unfortunately, after consecutive interventions patient died due to massive uncontrollable bleeding. Five-years follow-up, 67 patients were reached through telephone obtained from the hospital information system, and 42 patients were alive (62.8%). Seven cases returned with local recurrence, 5 in the renal fossa, and 2 in the abdominal wall. Five cases developed distant metastasis. The mortality rate in our study was 37.2%. 56% (14/25) of the cases died within 2 years, primarily in patients with a higher stage, a higher grade, and distant metastasis at the time of diagnosis; 11 patients died within 5-years postoperatively.

Table 1 Sociodemographic Characteristics of the Patients

Variables	No. of the Patients		Percentage, %
Age categories			
<18 years	6		7.1%
19–39 years	5		6%
40–59 years	32		38.1%
>60 years	41		48.8%
Gender			
Male	57		67.9%
Female	27		32.1%
Comorbidities	Yes	No	
Smoking	13	71	15.4%
Hypertension	16	68	19%
Diabetes	24	60	28.6%
Obesity	21	63	25%
Site of the Tumor			
Right	48		57.1%
Left	34		40.5%
Bilateral	2		2.4%
Location of the Tumor			
Upper pole	16		19%
Mid pole	12		14.3%
Lower pole	16		19%
>1 pole	40		47.6%

Table 2 Radiological and Histopathological Features of the Cases

Variable	No. of Patients	Percentage %
Tumor stage		
T1a	10	11.9%
T1b	8	9.5%
T2a	26	31.0%
T2b	16	19.0%
T3a	6	7.1%
T3b	3	3.6%
T3c	2	2.4%
T4	13	15.5%
Lymph node involvement		
Yes	27	32.1%
No	57	67.9%
Distant metastasis		
Yes	22	26.2%
No	62	73.8%
Type of RCC		
Clear cell	57	67.8%
Papillary	13	15.6%%
Chromophobe	6	7.1%
Unclassified RCC	8	9.5%
Grade		
Grade 1	6	7.1%
Grade 2	37	44%
Grade 3	17	20.2%
Grade 4	24	28.7%

Assessment of gender variation of tumor stage, grade, and comorbidities revealed a statistically significant difference between the pattern of stage and grade of RCC and gender group (Table 3). More than eighty percent of females had a low-stage and a low-grade RCC, while males held higher stages and higher grades RCC in 37% and 63%, respectively ($p<0.001$). Smokers were male-only, while obesity was common in female patients ($p=0.02$).

Our review showed that 54.5% (6/11) and 73.9% (54/73) of patients younger than 40-years and elderly patients had localized RCC. Clinically symptomatic cases were predominantly patients younger than 40-years compared to older patients, 78% versus 55%, respectively.

Discussion

There is a scarcity of studies in the body of the literature regarding renal cell carcinoma reported from Sub-Saharan Africa (SSA) including Somalia. There were eleven published studies from Nigeria, Senegal, Benin, and Togo that contained 482 patients with RCC.[13] There have been no previous studies reported from Somalia regarding the prevalence, clinical and histopathological features of renal cell carcinoma. This study is aimed to evaluate the epidemiological and histopathological characteristics of renal cell carcinoma at a tertiary hospital in Somalia.

RCC incidence rates differ significantly around the world. North America has the highest estimated incidence globally (12/100 000), with 1.8% and 0.9% cumulative risks for males and females. Western Europe (9.8) has the highest incidence rates for both sexes in Europe, while Africa has the lowest incidence and mortality rate, below 0.2% cumulative risks for both sexes.[14] RCC in the pediatric population is rare and accounts for 2% to 6% of malignant renal tumors.[15] The prevalence of RCC in our study was 0.7%, and 6 cases were pediatric age group.

Table 3 Gender Variation of Tumor Type, Stage, Grade, and Associated Comorbidities

	Male	Female	P-value
Age categories			
<18 years	4	2	0.725
19–39 years	4	1	
40–59 years	20	12	
>60 years	29	12	
Comorbidities			
Smoking	13	0	0.02
Hypertension	9	7	
Diabetes	15	9	
Obesity	7	14	
Type of RCC			
Clear cell	38	19	0.163
Papillary	9	4	
Chromophobe	5	1	
Adult, NOS	5	3	
T stage			
Stage 1	12	6	<0.001
Stage 2	24	18	
Stage 3	9	2	
Stage 4	12	1	
Grade			
Grade 1	2	4	<0.001
Grade 2	19	18	
Grade 3	13	4	
Grade 4	23	1	

The peak incidence of renal cell carcinoma appears between the sixth and seventh decade of age, with a median age of 64 years, and primarily is a disease of the elderly. The mean age of the patients in our study was 53.74±5.5 years. In discrepancy to sub-Saharan African countries, the mean age of the patients was 47.4 years, demonstrating early age incidence of the disease.[13]

There is a male predominance of renal masses with a 3:2 ratio of male to female, as stated in the European association of urology guidelines on renal cell carcinoma.[16] In contrast to the pooled analysis of data from sub-Saharan African countries, except for two studies (Benin 1.6:1, Nigeria 13:5 male-to-female ratio), there was a female predominance of RCC in 57.2% of the cases compared to males in 42.8%.[17,18] The current study noticed a 2:1 male-to-female ratio of renal mass, showing more than twofold male predominance.

In our study, most of the masses were in the right kidney, which aligns with a study reported by Muhammed A et al, who conducted a 10 years retrospective study in Nigeria and observed right-side predominance in 68.6%.[19]

More than 90% of RCC histological subtypes are clear cell, papillary, and chromophobe. Clear cell RCC represents 75% of RCC cases and is the most common and aggressive type, while papillary RCC accounts for 10%; and has a better survival rate than the clear cell. Chromophobe RCC accounts for 5% and carries the best prognosis rate and the lowest metastatic rate in only 7% of cases.[12] Our cohort revealed that clear cell RCC was the most common histological type, followed by papillary RCC. Regarding the comorbidities, 28.6% had diabetes, 25% were obese, 19% of the patients had hypertension, and 15.4% were smokers. To date, smoking, obesity, and hypertension are the consistent risk factors for RCC.[14]

About 20–30% overall recurrence rate after nephrectomy was reported depending on the clinical stage and grade, while the 5-year risk of recurrence in several retrospective studies has shown 60% in high-risk patients and 7–10% in low-risk patients. About 8.3% of our cases returned with local recurrence.[20] Most of the patients do not return with follow-up with medical imaging due to the inability to access the health facility, shortage of tertiary centers, far distance from health services, and the low socioeconomic state of our people. In a retrospective study of 74 RCC patients from Senegal over a nine-year, B. Fall et al reported a 12% tumor recurrence and 47.3% cancer-specific mortality rate, which is compatible with the present study.[21]

The 5-year survival rate for stage I is 93%, stage II/III is 72.5%, and stage IV only for 12%. A multi-institutional large retrospective study of 5670 patients over 36 years who underwent radical or partial nephrectomy from seven Latin American countries and Spain reported by Zequi et al found the 5-year survival for RCC to be 86.1%.[22] The five-year survival rate of our study was 62.8%, which is lower than the survival rate mentioned above. About 26.2% of the cases were diagnosed with metastatic disease, and a further 6% progressed to metastatic cancer despite surgical resection.

Most of the data reported from SSA have shown locally advanced to metastatic disease presentation. Only SALAKO from Nigeria and Tengue from Togo reported that 60.8% and 47.1% of the cases had localized RCC.[18,23] Seventy-one percent of our patients presented with localized RCC. Fifty percent of the patients in this study held tumor stage 2, followed by T1 in 21.4%, 15.5% in T4, and 13.1% in T3, which is in contrast to most of the studies reported from SSA. Tijani from Nigeria reported that most of his cases bore T3 in 39 (60.9%) and T4 in 21 (32.8%) of patients.[24] 58% had T4, and 21% had T3 in a retrospective study reported by MBAERI TU and associates.[25]

Our cohort revealed that 54.5% of patients younger than 40-years had localized RCC, with clinically symptomatic cases predominantly patients younger than 40-year. A 10-year retrospective Indian study, which included 198 patients (n=36, 18% <40 years and n=162, 82% older patients) reported that 63.8% of younger patients were diagnosed with RCC stages 1 and 2.[26] Another 10-year review study of 445 (n=104, 23% patients 40 years or younger) presented that younger patients had more aggressive diseases such as positive lymph node and metastasis at the time of diagnosis.[27] The present study showed that the rate of young patients was 13%. The previously reported rate ranges between 3% and 7% in patients <40-years. However, an increasing incidence rate in this age group was observed in the last decades compared to older patients.[28]

The mean tumor size in our research was 6.38±2.4 cm. Four SSA publications reported an average tumor size of 15.1 cm.[29] Most RCC cases in developed countries are discovered incidentally on imaging based on ultrasound and computed tomography of the abdomen. The survival rate is highly dependent on the stage at diagnosis, with metastatic disease having the least survival rate of about 12% at five years.[12] Due to less access to the health services and facilities, the absence of the awareness of the population, deficiency of well-equipped hospitals, rural distribution, and poverty status of the patients living in low-income countries lead to present with late and advanced disease.

Strengths and Limitations

1) this is a single-center-based study, although it is the sole tertiary and referral hospital and the only cancer center. 2) The study misses several factors such as lifestyle habits and occupational exposures. 3) No molecular biology and adjuvant chemotherapy available in Somalia. The present study is the first report regarding the prevalence, clinical and histopathological features of RCC in Somalia. We believe that the results of this study provide a significant contribution to global RCC incidence and mortality.

Conclusion

The study findings showed a satisfactory outcome, 71.4% of our patients presented with localized RCC, the five-year survival rate of the patients was 62.8%, and the mortality rate was substantially higher for patients with a higher stage, a higher grade tumor, and metastatic disease at the time of diagnosis. The prevalence of RCC in our study was 0.7%, and 6 cases were pediatric age group. Less access to the health services and facilities, the absence of the awareness of the population, limited availability of endourological equipment, inadequate expertise and imaging modalities, a far distance from health services, and the low socioeconomic status lead to most of the patients living in low-income countries presenting with advanced diseases.

Abbreviations

ISUP, International Society of Urologic Pathology; ICD, International Classification of Diseases; HIS, hospital information system; RCC, renal cell carcinoma; SSA, Sub-Saharan Africa; WHO, World Health Organization.

Data Sharing Statement

Data included in the manuscript.

Institutional Review Board Statement

The ethical research board committee of Mogadishu Somalia Turkish Training and Research Hospital (REF. MSTH-9006) approved the research. This study was carried out in accordance to the Helsinki Declaration contents.

Informed Consent Statement

All study participants and a parent of participants under 18 years of age previously consented to use their medical and surgical data in this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest associated with this publication.

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