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Clinical- pathological features and surgical outcome of renal cell carcinoma: Experience from a zonal referral hospital-northern of Tanzania

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Abstract

Background: Renal cell carcinoma (RCC) is the most common primary malignant tumour of kidney in adults. Recent studies from developed countries have shown that most renal tumour are currently diagnosed incidentally during screening for other disease which leads to better prognosis while few studies done in Africa still shows significant proportion of patients present with classic triad (>10%) which is a sign of advanced disease.

Objectives: This study aimed at determining clinical pathological feature and outcome of RCC in Northern zone of Tanzania.

Patients and Methods: This was a hospital based descriptive retrospective cohort study conducted at Kilimanjaro Christian Medical (KCMC) from January 2002 to December 2017. Data were analysed using statistical package for social science (SPSS) version 16. 0 and summarized in tables and figures.

Results: Forty three patients (43) underwent radical nephrectomy for RCC during the study period. Male to female ratio was1. 7: 1 with mean age of 53+/- 12 years. Flank pain (84%), abdominal mass (76%) and hematuria (44%) were the most common clinical presentation while classical triad was found in 40%. The most common clinical tumor stage was T3(72. 1%) whilst clear cell carcinoma was the commonest histological pattern. Five years survival length for T1, T2, T3 and T4 were 100%, 62. 5%, 32. 3% and 0% respectively.

Conclusion: The most common presenting symptom of RCC in our centre is flank pain, and abdominal mass. Majority of the patients presented with advanced disease with less than five year survival rate. Clear cell type was the predominant histological type.

Keywords: Renal cell carcinoma; Radical nephrectomy; Histopathology; Surgical Outcome; Tanzania

1. Introduction

RCC accounts for 2% to 3% of all adult malignant neoplasm while accounting for 85% of all kidney cancer and the remainder being urothelial cancer of renal pelvis Transitional Cell carcinoma [1]. It is believed to be rare in African and Asian and more prevalent in the United States [2]. Previous study in Tanzania showed that RCC accounted for about 9%

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of all urological malignances where females were the majority at54% while studies done by Klufio et al in 2004 reported that it accounted for 10. 4% of all urogenital tumors in Ghana [3,4].

Studies in developed countries shows that more than 70 % of renal cell carcinoma are diagnosed incidentally by imaging due to screening of other abdominal complains, while in Africa majority of tumor are diagnosed at advanced stage [5]. Furthermore, there is a limited options of treatment for RCC in Africa especially for advanced disease with new treatment modality such as immunotherapy and vascular-targeted therapy not available in most part of Africa including Tanzania. Furthermore, late diagnosis has been reported to result in poor prognosis in this part of the world compared to Western world [5].

There is scarcity of information about clinical presentation, pathologic patterns and surgical outcome of patients with adult RCC in East Africa. We conducted a retrospective hospital based descriptive cohort study to determine clinical presentation, pathologic patterns and surgical outcome of RCC at KCMC.

2. Material and methods

A retrospective hospital based descriptive cohort study was conducted between January 2002 to December 2017 at KCMC, which is a zonal, referral and teaching hospital of KCMUCo in Northern zone of Tanzania. According to the protocol of urology department of KCMC, RCC patients are followed up post operativelyevery3 months for the first year and then every 6 months in the second year and then annually for the rest of their life. During follow up, history and physical examination is done. Furthermore, renal function and routine ultrasound every 6 months is done for first two years and then annually thereafter.

File numbers of all adult patients who underwent nephrectomy for renal tumor were obtained from urology theatre registry book, there after their files were traced from medical records. Patients who had a proof histologically to have RCC post operatively were included in this study after a review of the slide by two pathologists. Information necessary for this study were extracted from their respective files and included age, sex, area of residence, occupation, clinical presentation, investigations done, clinical stage, surgical option, surgical complication, histopathological pattern and survival length.

Classification was done according to international tumor, node and metastasis (TNM) system for staging RCC proposed by American Joint Committee for cancer in 2009.

Patients' records-were reviewed retrospectively to note findings in the respective follow up period.

3. Results

3.1. Clinical presentation

A total of 43 patients had renal tumor and underwent nephrectomy during the study period. Out of 43 patients, 27 (67. 8%) were male with sex ratio of 1. 7: 1. Majority (65. 4%) were aged more than 50 years with mean age of 53. 91+/-12 years (table 1).

Majority presented with flank pain (84%) while abdominal mass and hematuria were 32(76%) and 19(44%) respectively. Classical triad of flank pain, hematuria and abdominal mass was found in 17(40%). About half 22(51. 2%) of the tumor was found to be on the right side. Only 14 patients (33%) presented with other systemic symptoms (B symptoms) such as weight loss, lower limbs oedema, lyphadenopathy, bone pain and persistent cough (Table 1).

Table 1 Clinical characteristics of participants

Parameter Frequency (n=43)		Percentage (%)
Age Categories (years)		
31-40	9	20. 9
41-50	6	14. 0
51-60	13	30. 2
61-70	11	25. 9
Above 71	4	9. 3
Mean 53. 91(Range 32-76)		
SD+/-12. 49		
Sex		
Male	27	62. 8
Female	16	37. 2
M: F	1. 7:1	
Symptoms		
Flank Pain	36	84. 0
Abdominal mass	32	76. 0
Hematuria	19	44. 0
Classic Triad	17	40. 0
B symptoms	14	33. 0
Kidney involved		
Right	22	51. 2
Left	21	48. 8

Majority of patients had clinical tumor stageT3(72. 1%) followed by T2b(18. 5%)(Table 2).

Table 2 Tumor characteristics of RCC (N=43)

TNM Stage	N	%
T Stage		
Tx	0	0. 0
T1a	0	0. 0
T1b	2	4. 7
T2a	3	7. 0
T2b	5	11. 5
T3a	9	20. 9
T3b	14	32. 6
T3c	8	18. 6
T4	2	4. 7
N Stage		
Nx	16	37. 2
N0	25	58. 1
N1	2	4. 7
M Stage		
M0	43	100. 0
M1	0	0. 0

3.2. Pathological patterns

Clear cell carcinoma was the commonest histopathological pattern in 33(79%) followed by papillary 7(16. 3%) and unclassified type 3(7%)(Table 3) .

Table 3 Histopathological Patterns (N=43)

Histopathological Type	n	%
Clear cell	33	76. 7
Papillary	7	16. 3
Unclassified	3	7. 0

3.3. Surgical outcome

All 43 patients underwent only nephrectomy as the treatment for RCC. Postoperatively, surgical site infection was noted in 2(4. 6%) patients. There was no case of metachronous tumor.

Table 4 Type of nephrectomy and follow up(N=43)

Parameter	n	(%)
Type of Open Nephrectomy		
Radical Nephrectomy	43	100
Partial Nephrectomy	0	0
Follow up post RN		
Lost to follow up before 12 month post RN	7	16. 3
Followed up for 5yrs post RN	36	83. 7

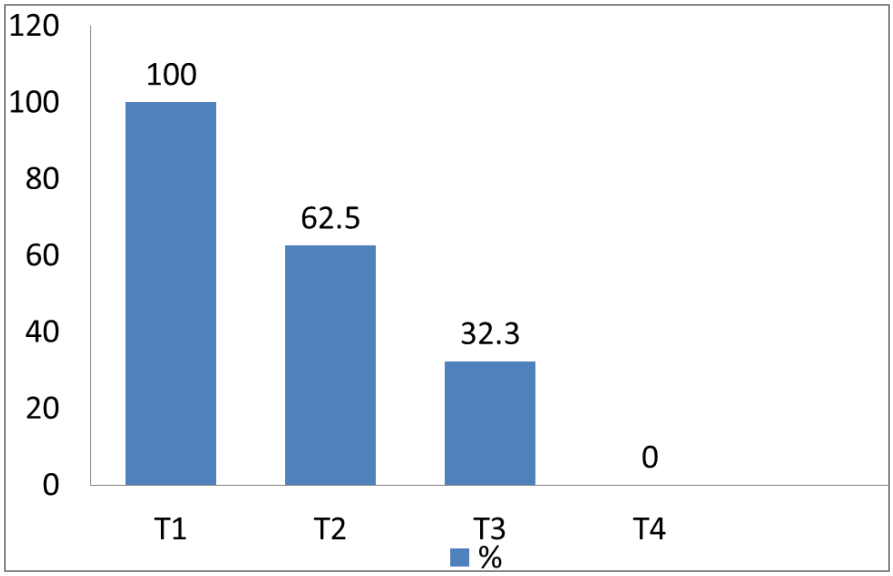

Figure 1 5-year survival by T-Clinical stage (N=17)

Average follow up was 12 months (range 3-52 months) and 7(16. 3%) patients did not come for follow up after 12 months post nephrectomy. Among available follow up beyond 12 months post nephrectomy were 36 patients, only 17(47. 2%) were alive at firth year of follow up, where by all patient 2(100%) who had T1 tumor were alive at five years while for T3 disease, only 5(32. 3%) were still alive at year five of follow up (figure 1).

4. Discussion

The epidemiology, clinical presentation and surgical outcome between developed and underdeveloped countries is slight different because of early diagnosis due advancement in renal imaging and availability of targeted therapies and immunotherapy in their settings which may have influence on the outcome. Currently many renal tumors in developed countries are incidentally diagnosed.

In this study analysis of patient demographic features showed that sex distribution was almost twice as common in male than female with male to female ratio of 1. 7: 1. This was similar to other studies done by Lipworth *et al* in2006, 2011 [6,7] which showed male predominance with ratio of 3:2. But this was contrary to the study done in Nigeria by Muhammed *et al in* 2016 which showed RCC was almost twice common in female than male with male to female ratio of 1:1. 7 [8]. This difference could be due to differences in study population with different risk bahaviours/factors.

The peak age in this study was the 5th decade (Mean 53years) which is similar to findings in study done in Nigeria by Muhamed et aland South Africa by-Claassen*et al*in 2011 [8,9]. This is at least one decade earlier than in Western world population where RCC is primary disease of elderly with typical presentation in sixth and seventh decades. [1,10] This difference in demographic characteristics might be attributed to the difference in genetics, reproductive and hormonal factors, diet, environmental factors or simply underreporting and lower life expectancy among Africans.

Majority of the renal tumor presented on the right side that was similar to most other studies [5,11].

In this study flank pain was found in 84% followed by abdominal mass 76%and hematuria 44%. These findings were almost similar to studies done in Western Africa [5,8] but were different from findings obtained from other studies as hematuria was the commonest symptom followed by flank pain. [1,13]. The classic triad of flank pain, hematuria and abdominal pain that usually indicates incurable disease was found in 40% of the patients. This was almost similar to studies done in Nigeria [12] but it was very different from studies done in Pakistan by Ata-ur-Rehman *et al.* , 2015 and USA by Rini *et al.* , 2009where it's reported to be less than 10%. [1,13]. Early diagnosis as an incidental finding and good health seeking behaviours in developed countries help in early detection of RCC. This signifies that most of our patients presents at advanced stage when disease is incurable.

Regarding the histopathological patterns, this study showed similar patterns with other studies as clear cell types were the predominant histopathology in 76. 7%. While for the non clear cell types, papillary type accounts for16. 3% and unclassified types being 7%. This finding was similar to other studies whereby clear cell type was the most common subtype. [5,14]. Other subtypes like chromophobe and collecting duct were not detected in our study; it may be due to small sample size.

All patients in this study underwent radical nephrectomy. The reasons for this type of surgery were advanced disease, lack of laparoscopic facilities and laparoscopically trained surgeons at the hospital which is minimally invasive and offers equivalent oncological outcomes and improved postoperative outcomes compared to open nephrectomy. This was contrary to other studies where by partial nephrectomy was performed for localized tumor of less than 4 cm and radical nephrectomy for larger advanced tumor and both yield almost same oncological results [1,15].

In this study,16. 3% of patients lost follow up after 12 months post nephrectomy. Nearly half 17(47. 3%) patients were still alive at year five of follow up. The higher percentage of the loss of follow up was also noted in study done by Tijan et al in Nigeria as at 10 months [67%] patients were lost to follow-up. The lost to follow up can be due to ignorance on follow up benefits, economic issues, poor infrastructures and deaths which may have occurred due to either cancer itself as most of our patients presented with advanced disease stage or other conditions. [5]

The clinical stage, tumor size and grade are well known in predicting the surgical outcome and survival length. In this study tumor size and grade were not reported in almost all patients but clinical stage showed importance in survival length. Regarding the clinical stage, those few patients with localized disease had better survival length compared with advanced disease patients whereby among patient with T1 and T2 stage had put actual number (100%) and put actual number (62. 5%) year survival respectively. This was similar to study done by Zhou et al in China and Sweden by Ljungberg et alwhereby 5 years survival length was higher among T1 and T2 with 85. 5%-100 % and 69%-75% respectively [16,17]. This was quiet different in those patient with advanced disease from T3 as only 32. 3% patient had survival length of five years. This signifies clinical stage as the most important variable for prognosis and survival after surgery and very low 5 years survival length among our patients could probably mean they came late for treatment where surgery was done only with palliative intent or can be due to other unreported cormobidities during the cause of illness post nephrectomy.

As RCC being known to be chemo refractory and radiation resistant tumor, new management options for advanced and metastatic RCC have been developed such as immunotherapy and targeted therapy including vascular endothelial growth factor (VEGF) which have shown to increase survival length especially in developed countries [1, 17]. In this study though there were clear indications for the use of these agents by most patients due to advanced stage but the drugs were not readily available.

5. Conclusion

The most common presenting symptom of RCC in our centre is flank pain, followed by abdominal mass, with more than one third of the patients presenting with typical clinical trial. With regard to clinical tumor stage, majority present with advanced disease that resulted into less five-year survival rate. Clear cell type was the predominant histological type and all tumors were not graded. It was noted that significant number of patients did not come for follow up after 12 months post operatively.

Recommendations

We need to conduct a large prospective study in order to understand the reason for lost to follow up in these groups of patients. In this-prospective study we would also be in a position to know the duration of symptoms and possible reason for late presentation to the hospital.

We need to emphasis the importance of tumor grade in order for our colleague pathologist to grade all RCC accordingly

Although we did not study the effect of adjuvant therapy like immunotherapy and vascular targeted therapy in this study, it is well known that they have positive effect on the survival especially in patients with clear cell type of RCC. Therefore, we recommend that effort should be made by stakeholders to make the drugs available as most of our patients had papillary type and present with advanced disease and there for had less five-year survival rate.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that they have no competing interests.

Statement of ethical approval

Approval for this study was obtained from Kilimanjaro Christian Medical College Research Ethics Committee with reference number 2307 and permission to extract data from files was thought from Executive director of Kilimanjaro Christian Medical centre.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

List of Abbreviations

KCMC – Kilimanjaro Christian Medical Centre
RCC – Renal cell carcinoma
TNM – Tumour, Nodal , Metastasis
VEGF – Vascular Endothelial Growth Factor

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Authors' contributions

VK designed the study; JSM, AKM, FB, NBN and OJM gave inputs in the study design and conduct; VK did data collection and analysis AKM, FB, NBN, JSM and OJM input in the analysis; AKM, FB, NBN, JSM and OJM read the final manuscript for scientific content of the paper. All authors read and approved the final manuscript.

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