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# A CLINICO PATHOLOGICAL STUDY ON RENAL CELL CARCINOMA IN A TERTIARY CARE CENTER

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## ABSTRACT

**Background :**The incidence of renal cell cancer (RCC) is increasing worldwide. However, scant information is available from the India, about its clinicopathological characteristics and survival outcomes. We prospectively analyzed data of patients suffering from RCC at Department Urology, Andhra Medical College & King George Hospital, Visakhapatnam, from October 2015 to January 2018 to generate information on these aspects.

**Materials and Methods :** 32 patients treated between October 2015 to January 2018 were prospectively analyzed. Baseline characteristics, histopathological information, and survival outcomes were assessed.

**Results:** The peak incidence of RCC was seen in 5th decade followed by 4th decade. The mean age at presentation was 52.45 years. Incidence is higher in males than in females with a ratio of 2.3:1. Smoking is associated with 45% of cases and hypertension in 34% of cases. The classic triad of RCC was seen only in 3 cases (8%). The mean tumour size was 10.25cm, range 5-19 cm. Only 5% of tumours were of size less than 4cm. 31% cases were in stage 1, 30% in stage 2 , 31 % in stage 3 and 8% in stage 4. Tumours are localized in 57%, locally advanced in 31 % and metastatic in 9%.Partial nephrectomy was done in only 2(5%) cases . Open Radical nephrectomy was done in 85% of cases. Post op biopsy showed Clear cell RCC variant in 22 (68%) and papillary carcinoma in 7 (21%),multilocular cyst in 1 (3%) and malignant fibrous histiocytoma in 1 case(3%). 75% of cases showed Fuhrman's grade 2 and 25% showed grade 3. Capsular invasion was seen in 21% and lymph nodal positivity for metastatic deposits in 12% and 34% showed necrosis. 5 Deaths were noted. 3 cases missed the follow up after surgery. All cases were advised 6 monthly ultrasound abdomen and chest X ray.

**conclusions:** Younger age at presentation, higher male–female ratio, lower proportion of asymptomatic patients, higher proportion of advanced stage at diagnosis, smoking & hypertension more commonly associated with RCC. clear cell and papillary variants of RCC are more common.

## KEYWORDS

RCC, Clear cell variant, radical nephrectomy

## ARTICLE HISTORY

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## INTRODUCTION

Renal cell carcinoma (RCC) has emerged as one of the most rapidly evolving areas of solid tumor oncology. The past two decades have seen a dramatic change in the clinical landscape that shaped both RCC understanding and treatment. Development of minimally invasive techniques for surgery in the retroperitoneum, emergence of focal therapy, re-emergence of percutaneous renal biopsy, introduction of active surveillance strategies, renewed interest in immunotherapy, and the clinical development of targeted therapies for patients with advanced disease have revolutionized kidney cancer care.

Efforts aimed at morphologically grouping specific cancers into distinct pathologic subtypes have not only allowed a common descriptive language, but are helping to crystallize the understanding of RCC's molecular origins and its clinical behavior. Indeed, these improved insights into the similarities and differences among RCC variants should offer clinical and therapeutic opportunities to improve patient care.

RCC accounts for 2-3% of all adult malignant neoplasms and is the most lethal of the urological cancers[1]. In India the estimated incidence of RCC is 2 per 1 lakh in male and 1 per 1 lakh in females. Unfortunately the incidence of RCC is gradually increasing and despite a trend towards earlier detection mortality rate is steadily increasing[2]. The rising mortality rates are particularly troubling because the proportion of advanced tumours has actually decreased, which suggest a deleterious change in tumor biology.

Tobacco smoking, obesity and hypertesion are three major causative factors associated with RCC. Tobacco smoking use accounts for 20-30% of cases of RCC in men and 10-20% in women. Relative risk is directly related to duration of smoking and begins to fall after cessation. Potential mechanism linking obesity & RCC are increased insulin like growth factor-1 expression, increased circulatory estrogen levels, increased arteriolar nephrosclerosis, and local inflammation,. Hypertension induced renal injury and inflammation or metabolic or functional change in the renal tubules that may increase susceptibility to carcinogens.

Family history of RCC,[12] Regular usage of NSAIDS,[13]retroperitoneal radiation therapy[14] and occupational exposure all are associated with development of RCC. End stage renal disease has a relative risk of 5to20 fold[15]. RCC is common in low socio economic status and urban areas. Moderate alcohol consumption appears to have protective role for reasons not known.

## MATERIALS AND METHODS

Patients for this study have been selected from those attending Urology Department, King George hospital, Visakhapatnam, from October 2015 to January 2018. 35 patients of renal cell carcinoma have been studied of which 32 cases underwent surgical management. Patients attending urology department diagnosed to have RCC were included in the study . Urothileal malignancies of kidney were excluded.

An elaborate study of these cases with regard to history of onset of preset complaintnt, previous history, family history, occupational history, socio economic status was done. Duration and progression of various symptoms were documented. Complete physical examination was done. Complete evaluation was done in every case. No significant previous history of renal disease found except simple cysts and nephrolithiasis in 5 cases. Routine surgical profile along with serum electrolytes, serum calcium, ultrasound abdomen and CECT scan of abdomen were done. Metastatic work up like liver function tests, alkaline phosphatase, Chest X ray were done .CT chest was advised on basis of clinical suspicion.

MRI scan was advised in 3 cases with high serum creatinine for evaluation of tumour thrombus in vessels. Function of contralateral kidney was assessed based on available investigations and e-GFR. After Complete evaluation patients were staged according to TNM classification. Surgery was deferred for 3 patients and managed conservatively because of poor performance status and presence of CKD by the time of presentation.

All the remaining cases were staged pre-operatively and possibility of nephron sparing surgery evaluated with RENAL scoring system based on CECT findings. Most of the patients were given blood transfusion to improve general condition. Surgical options and mortality risks were explained to patients and consent taken before proceeding to surgery(Radical nephrectomy/partial nephrectomy). For Radical nephrectomy, all patients were given general anaesthesia. All tumours below T2 and without vascular thrombus were operated through 11th rib transcostal incision via retroperitoeally and those with T3 & above and tumours with thrombus in IVC were given mid line vertical abdominal incision and proceeded.

One patient of T2 tumour with simultaneous 3cm upper ureteric stone was operated through midline laparotomy incision and radical nephrectomy and ureterolithotomy done through the same incision. Tumours above 15 cm or large upper pole tumours were operated by thoraco abdominal incision from 8th intercoastal space and post operatively managed with underwater ICD tube.

Lymphadenectomy was done only if lymphnodes were found to be enlarged intra operatively and sent for HPE. Adrenal gland was preserved if possible. All resected nephrectomy specimens were examined in cut section and sent for histopathological examination

Patients of partial nephrectomy were operated through flank approach. After entering retroperitoneum, gerota's fascia opened, renal vessels clamped with satinsky clamps. mannitol infusion given before clamping. Kidney is cooled with ice slush for 20 minutes. partial nephrectomy with 1cm margin was done followed by capsular approximation with absorbable sutures over a haemostatic bolster.

All patients were followed up with 3 monthly USG scan of abdomen, followed by every6 monthly ultrasound. Yearly CECT scan of abdomen All patients were followed till end of study period and conclusions made accordingly.

Of the 32 patients operated 2 patients died. One patient within 1 year from presentation and another patient after 16 months from presentation. Both cases were in clinical stage T3b and post operatively biopsy suggestive of capsular invasion and perinephric fat invasion and sarcomatoid differentiation. Of the 3 cases managed conservatively, one case died within 8 months of presentation was in stage IV at presentation had liver metastasis and other 2 cases were followed for progression till date for 6 months found no progression of disease.

## OBSERVATION AND RESULTS :

The peak incidence of renal cell carcinomas in present sutdy was seen in 5th decade consisting of 15 (42.8%)patients, followed by 4th decade with 11 (31.4%) patients.The mean age at presentation was 52.45 years. Incidence of renal cell carcinomas is higher in males than in females with a ratio of 2.3:1. Proportion of female patients was more in younger age group. The renal cell carcinoma was more frequently located in the right kidney than on the left side by a ratio of 1.17: 1.
Smoking is associated with 45% of cases and hypertension in 34% of cases. The classic triad of RCC including flank pain, fever, mass per abdomen was seen only in 3 cases (8%). Flank pain is seen in 45% cases followed by weight loss (40%) and haematuria (34%). Mass per abdomen is seen in 17% of cases. Significant weight loss noted in 40% cases. Anaemia was noted in 13 (37%) cases and predominantly found in female population. Incidental presentation was seen in 22 % of patients. The mean tumour size was 10.25cm with range between 5-19 cm. Only 5% of tumours were of size less than 4cm. 31% cases were in stage 1, 30% in stage 2 , 31 % in stage 3 and 8% in stage 4. Two cases (5%) presented with synchronous metastasis. Tumours in present study are localized in 57%, locally advanced in 31 % and metastatic in 9%.

### Type of Surgery performed :

| Surgery | Number | % |
|---|---|---|
| Partial nephrectomy | 2 | 5 |
| Radical nephrectomy | 30 | 85 |
| IVC thrombectomy | 2 | 5 |
| Non-surgical management | 3 | 8 |

### Type of surgery performed in the present study

Only 2(5%) cases in present study were T1a tumours and partial nephrectomy was done in these cases. Open Radical nephrectomy was done in 85% of cases. 10 cases of radical nephrectomies were operated through 11 rib approach and 9 cases through thoraco abdominal approach and 11 cases were operated through midline laparotomy incision. IVC thrombectomy was done in 2 cases, both were of level 2 IVC thrombus..

### Pathological sub types :

| Sub type | Number | % |
|---|---|---|
| Clear cell carcinoma | 22 | 68 |
| Papillary carcinoma | 7 | 21 |
| Multilocular cystic carcinoma | 1 | 3 |
| others | 1 | 3 |

### Pathological distribution of RCC

Clear cell RCC variant was seen in 22 (68%) and papillary carcinoma in 7 (21%) and multilocular cystic in 1 (3%) and malignant fibrous histiocytoma in 1 case(3%).

### Prognostic factors in RCC :

| Prognostic factors | Number | Present study% |
|---|---|---|
| Fuhrmans grade 2 | 24 | 75 |
| Fuhrmans grade 3 | 8 | 25 |
| Capsular invasion | 7 | 21 |
| Sarcomatoid differentiation | 3 | 9 |
| Perinephric invasion | 5 | 15 |
| Lymph nodal positive | 4 | 12 |
| necrosis | 11 | 34 |

Post operative biopsies of all patients were evaluated for prognostic factors. 75% of cases showed Fuhrman's grade 2 and 25% showed grade 3. Capsular invasion was seen in 21% and lymph nodal positivity for metastatic deposits in 12% and 34% showed necrosis. Few

patients had foci of calcifications and 10 cases showed evidence of chronic pyelonephritis in surrounding parenchyma. 5 Deaths were noted. 3 cases missed the follow up after surgery. All cases were advised 6 monthly ultrasound abdomen and chest X ray.

## DISCUSSION

The peak incidence of RCC was seen in 5th decade consisting of 15 (42.8%) patients, followed by 11 (31.4%) patients in 4th decade which is similar to the study by Agnihotri et al17 in india and in contrast to a study by Ac stinga and kwang park et al18 where incidence is peak at 6th decade followed by 2nd peak in 5th decade indicating earlier presentation in present study .

In a study from Surveillance Epidemiology and End Results (SEER) database, majority of RCC cases at presentation were between 60-69 or 70-79 yr of age and only 42 per cent of patients presented in < 60 yr of age. In the present study, 82.7% of patients were below the age of 60 year.40% of patients in the present study were under 50 years which is close to 30.03% in a study by Agnihotri et al17.The mean age at presentation was 52.45 years in present study where as it was 60.79 years in a study by Kwang et al18 and was 56 years in a study by Yuvaraja et al[19].

Incidence of RCC is higher in males than females with a ratio of 2.3:1 comparable to male to female ratio of 1.6:1.0 in a study by Kwang et al18.This difference in sex ratio may reflect the difference in perception in seeking health care for a male and a female member of the family looking at the limited financial resources in a developing country like India. The renal cell carcinoma was more frequently located in the right kidney than the left by a ratio of 1.17: 1 which is different from 1:1.25 from a study by Kwang et al[18].

Smoking is associated with 45 % of cases and hypertension in 34 %of cases which is slightly higher when compared to other studies stating smoking, hypertension, obesity all together are associated up to 49% only. The classic triad of RCC i.e. flank pain, fever & mass per abdomen were seen only in 3 cases (8%) is comparable to < 10% as stated by study from Rini et al2. Flank pain is seen in 45% cases followed by weight loss (40%), haematuria (34%) mass per abdomen is only seen in 17% of cases. Flank pain being the most common presentation seen in 45% of cases is higher when compared to other studies Waters et al21 (38%) and Jacobs et al22 (21%) Virdi et al23 (28%).

Haematuria seen in 34% of cases is lower than the above mentioned studies where it is around 50%.Significant weight loss noted in 40% is similar to Virdi et al23. Mass per abdomen in 17% is similar to other studies. Anaemia noted in 13 (37%) cases and predominantly found in female population. Anaemia mentioned in many studies as feature of advanced RCC could not be concluded from the present study. Incidental presentation was22 % in present study which is comparable to study by Mevorach et al24 29% and Thompson 25 and peek 18%. Elevated serum creatinine was noted in 5 cases which were proceeded with eGFR calculation. 3 cases died within one year of diagnosis. No treatment was offered because of their poor performance status and poor compliance.

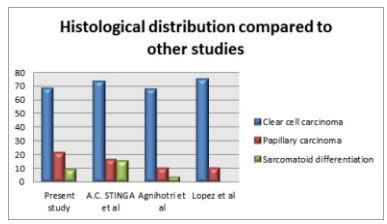
The mean tumour size was 10.25cm with range between 5-19 cm in present study and predominantly right sided and similar to mean size of 8.08cm in study by Agnihotri et al[17].

As stated by few studies that tumours frequently originate from upper and mid pole, differentiation could not be made about the site of origin within the kidney as most of the masses were bigger in size involving most portion of kidney.

Only 5% of tumours in present study were of size less than 4cm, where as it is 10.4 % in study by Agnihotri17. 31% cases in present study present in stage 1 and 30% in stage 2 and 31 % in stage 3 and 8% in stage 4 which is different when compared to 50%, 10%,16%, 24% in a study conducted between 1993-2004 which showed an increasing trend in stage 1 and declining trend of stages 2,3,426. 2 cases (5%) presented with synchronous metastasis in present study which is comparable to 2% in Thompson et al and 8% in virdi et al[23].

Tumours in present study are localized in 57% , locally advanced in 31 % and metastatic in 9% and these values are similar to study by Rini20 and Antonio et al. O dea et al liver metastasis (6%) and adrenal 11%. Hatcher et al27 - Renal vein spread is noted 12% and IVC 9%. Schwerk et al28- renal vein spread is noted 18% and IVC 11%.

Clear cell carcinoma seen in 68% of cases is similar to study by Agnihotri et al17 (67.7%) and close to study by Ac Stinga29 et al (73%). Papillary carcinoma is seen in 21% which is close to Agnihotri17 et al (16%) and close to other studies by Ac stinga29 . Sarcomatoid differentiation is seen in 3cases (9%) of clear cell carcinoma which is close to 15% in study by Ac Stinga29 and higher when compared to other 2 studies mentioned above where it is only 3% and 5% in study by Antonio et al.[17]




75% of cases showed Fuhrman's grade 2 and 25% were grade 3. capsular invasion was seen in 21%. And lymph nodal positive for metastatic deposits in 12% and 34% showed necrosis. Few patients had foci of calcifications and 10 cases showed evidence of chronic pyelonephritis in surrounding parenchyma.

## CONCLUSIONS:

Present study gives an insight into age, gender, stage and pathological subtype of RCC. RCC is common in males, 5th decade being most common age group followed by 4th decade with mean age of 52.45 years at presentation which shows an earlier onset compared to western countries. Smoking and hypertension are associated with RCC. Asymptomatic presentation seen in 22%, classical triad of RCC is not common, most common presentations are pain, weight loss, haematuria and anaemia. Equal presentation among Stages 1,2,3 were noted with only 5% were T1a tumours and mean tumour size was 10.25cm, radical nephrectomy was the common procedure done. Staging with CT scan correlated with pathological stage except for venous thrombus. majority of cases were of Clear cell RCCs variant, was seen in [22] ([68]%) followed by papillary carcinoma ([21]%) and multilocular cystic in [3]% and malignant fibrous histiocytoma in [3]%. On HPE Fuhrman's grade 2 is common (75%), sacomatoid differentiation (9%) seen in clear cell variant, necrosis (34%) and peri tumoural changes of chronic pyelonephritis is common 30%. Recurrence rate or metastasis was seen in 9.5% with follow up period of 2 years. Recurrent or metastasis cases have poor prognosis and palliation is better than systemic therapies. 5 patients died in follow up period. Survival rates could not be evaluated because of short duration of study. Because of rare incidence of RCC screening is not advisable.

## REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin 2013; 63: 11–30.
2. Chow WH, Devesa SS, Warren JL, et al. Rising incidence of renal cell cancer in the United States. JAMA 1999; 281: 1628–31.
3. Wallen EM, Pruthi RS, Joyce GF, Urologic Diseases in America Project, et al. Kidney cancer. J Urol 2007; 177: 2006–19.
4. Decastro GJ, McKiernan JM. Epidemiology, clinical staging, and presentation of renal cell carcinoma. Urol Clin North Am 2008; 35: 581–92.
5. Hock LM, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: an analysis of surveillance, epidemiology and end results program data. J Urol 2002; 167: 57–60.
6. Kane CJ, Mallin K, Ritchey J, et al. Renal cell cancer stage migration: analysis of the National Cancer Data Base. Cancer 2008; 113: 78–83.
7. Hunt JD, van der Hel OL, McMillan GP, et al. Renal cell carcinoma in relation to cigarette smoking: meta-analysis of 24 studies. Int J Cancer 2005; 114: 101–8.
8. Ljungberg B, Campbell SC, Choi HY, et al. The epidemiology of

renal cell carcinoma. Eur Urol 2011; 60: 615–21.
9. Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371: 569–78.
10. Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. Nat Rev Cancer 2004; 4: 579–91.
11. Lipworth L, Tarone RE, McLaughlin JK. The epidemiology of renal cell carcinoma.J Urol 2006; 176: 2353–8.
12. Gago-Dominguez M, Yuan JM, Castelao JE, et al. Family history and riskof renal cell carcinoma. Cancer Epidemiol Biomarkers Prev 2001; 10: 1001–4.
13. Cho E, Curhan G, Hankinson SE, et al. Prospective evaluation of analgesic use and risk of renal cell cancer. Arch Intern Med 2011; 171: 1487–93.
14. Romanenko A, Morell-Quadreny L, Nepomnyaschy V, et al. Pathology and proliferative activity of renal-cell carcinomas (RCCs) and renal oncocytomas in patients with different radiation exposure after the Chernobyl accident in Ukraine. Int J Cancer 2000; 87: 880–3.
15. Farivar-Mohseni H, Perlmutter AE, Wilson S, et al. Renal cell carcinoma and end stage renal disease. J Urol 2006; 175: 2018–20.
16. Bellocco, R., Pasquali, E., Rota, M. et al. Alcohol drinking and risk of renal cell carcinoma: results of a meta-analysis. Ann Oncol. 2012; 23: 2235–2244.
17. Agnihotri S, Kumar J, Jain M, Kapoor R, Mandhani A. Renal cell carcinoma in India demonstrates early age of onset & a late stage of presentation. Indian J Med Res. 2014; 140(5): 624-629.
18. Kwang Hwa Park, Dong Hwan Shin, In Joon Choi. A Pathological Study of Renal Cell Carcinoma. The Korean Journal of Pathology 1989; 23(3): 322-330.
19. Yuvaraja, T. B. et al. "Genitourinary Cancers: Summary of Indian Data." South Asian Journal of Cancer 5.3 (2016): 122–124. PMC. Web. 8 Feb. 2018. Brian I Rini
20. Brian I Rini, MD Active surveillance in metastatic renal-cell carcinoma: a prospective, phase 2 trial. Lancet Oncol. 2016 Sep; 17(9): 1317-24. doi: 10. 1016/S1470-2045(16)30196-6. Epub 2016 Aug 3.
21. Waters WB, Richie JP. Aggressive surgical approach to renal cell carcinoma: review of 130 cases. J Urol1979; 122(3): 306-9.
22. Jacobs SC, Berg SI Lawson RK.Synchronous bilateral renal cell carcinoma: total surgical excision. Cancer 1980; 46(11): 2341-5.
23. Virdi JS, Keely DG.Prognostic value of renal venous involvement in renal cell carcinoma.Br J Urol1992; 69(5): 481-5.
24. Mevorach RA, Segal AJ, Tersegno ME, Frank IN. Renal cell carcinoma:incidental diagnosis and natural history: review of 235 cases.Urology 1992; 39(6): 519-22.
25. Thompson IM, Peek M. Improvement in survival of patients with renal cell carcinoma- the role of the serendipitously detected tumour.J Urol 1988; 140(3): 487-90.
26. Christopher J. Kane, MD1,2 Katherine Mallin, PhD3 Jamie Ritchey, MPH3 Renal cell cancer stage migration: Analysis of the National Cancer Data Base
27. Hatcher PA, Anderson EE, Paulson DF, Carson CC, Robertson JE. Surgical management and prognosis of renal cell carcinoma invading the vena cava.J Urol 1991; 47(4): 216-18.
28. Schwerk WB, Schwerk WN, Rodeck G.Venous renal tumor extension: a prospective US evaluation.Radiology. 1985 Aug; 156(2): 491-5.
29. A. C. Stınga, A. S. Stınga, C. Simionescu, C. M ˘ arg ˘ aritescu, and ˘ M. Cruce, "Histopathological study of renal cell carcinoma," Current Health Sciences Journal, vol. 35, no. 1, pp. 52–57, 2009.