Original Article

Renal cell carcinoma: epidemiology, risk factors and clinicopathological profile

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ABSTRACT

Background: *The incidence of renal cell carcinoma (RCC) is increasing worldwide. The aims of this study were to describe epidemiological data, risk factors, clinicopathological characteristics of RCC.*

Methods: *This cross-sectional descriptive study was carried out at the department of Urology, BIRDEM General Hospital from Janaury 2013 to July 2023. All radiological characteristics and fine needle aspiration (FNA) positive RCC cases were included and othere renal tumor such as angiolipoma, renal cyst, renal tuberculosis were excluded.*

Results: *A total 200 RCC patients were included in the study. The mean age at presentation was 52.28 years and male (74%) were predominant. Most of the patients (66%) were asymptomatic, smoking (62%) was the most common modifiable risk factor, 50% patients had hypertension. In 54% cases right kidney was involved. Raised erythrocyte sedimentation rate was the most common (60%) paraneoplastic feature. The most common histopathologic type of renal tumour was clear cell carcinoma (70%), followed by papillary (20%) and chromophobe (6%) carcinoma; 66% of the patients presented at Robsing Stage II and 20% cases diagnosed as stage III.*

Conclusion: *It had been observed that RCC mostly occurred in young male patient at right kidney with fewer symptomatic detection. Tobacco smoking were the most common modifiable risk factor. Diagnosis were made at advance stage of the disease.*

Key words: *renal cell carcinoma, kidney cancer, stage, treatment.*

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INTRODUCTION

Renal cell carcinoma (RCC) accounts for 3% of all adult cancers and 85% of all kidney tumour.[1] Incidence of RCC is lower in Asian region, particularly in this subcontinent, probably due to lack of reporting.[2] Nonetheless, incidence is currently increasing at a rate of 2% per year in many developed countries.[3,4] Its frequency is also expected to rise in our country due to

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increasing life expectancy, rising awareness, better diagnostic facilities and growing prevalence of risk factors such as obesity.[5] However, there is a paucity of data for RCC from the Indian subcontinent.[6,7] Hence, to generate more information we prospectively analyzed data of 200 consecutive patients with RCC treated over 10 years.

METHODS

This was a cross-sectional descriptive study with the patients of RCC presenting in urology department, Bangladesh institute of Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital from January 2013 to July 2023. All fine needle aspiration cytology (FNAC) positive and radio logically suggestive RCC were included here and other renal tumours diagnosed as angiolipoma, renal cysts were excluded. Laboratory investigations including tests for paraneoplastic syndrome (PNS), were performed. Treatment was offered according to the stage of the disease and available treatment modalities. The seventh and eighth edition of the American Joint Committee on Cancer tumour, nodes and metastasis (TNM) staging systems were used to classify cancer stage and grade.[8] The histological subtypes were classified as per the classification of World Health Organization for renal tumours, 2016.[9] Both qualitative and quantitative data were collected using questionnaire devised for the study.

RESULTS

Total patients were 200 with a mean age at diagnosis 52.28 (35 - 78) years and RCC was more in male (148, 74%). Age distribution is shown in Table I. Smoking (62%) was the most common modifiable risk factor (Table II). Hypertension (50%) was the most common associated medical condition. In 54% cases of RCC, lesion was in right kidney and 46% in left kidney. In 54% cases RCC was in upper pole and in 46% in lower pole. In our study, 66% patients were diagnosed incidentally, 22% presented with pain and heamaturia and 12% with loin mass (Table III). Sixty percent patients had raised erythrocyte sedimentation rate (ESR), 40% cases had anaemia, 15% cases had weight loss, 2% had pyrexia and 2% had hypercalcamia (Table IV). Regarding tumour size, 60% were between 3-7 cm, 30% were more than 7 cm and 10% were less than 3 cm. Two-thirds (66%) of patients were in Robsing Stage II, 20% stage III, among these 8% had renal vein or inferor venacaval involvemant and 12% had nodal involvement, 12% of tumour were of stage I and 2% were stage IV disease (Figure 1). Most (140, 70%) cases were diagnosed as clear cell sub-type, 40 cases (20%) were papillary sub-type, 12 cases (6%) were chromophobe and 8 cases (4%) others (such as collecting duct, medullary carcinoma, renal cell carcinoma unclassified) (Figure 2).

Table I. Age distribution of the patients (N = 200)

Age (years)	Frequency	Percentage
35-45	12	6
46-55	140	70
56-65	28	14
66-75	16	8
>75	4	2

Table II. Risk factors for renal cell carcinoma (N = 200)

Risk factors	No of patients	Percentage
Modifiable factors		
Smoking	124 (All are male)	62
Excess body weight	24	12
Alcoholic	4	2
Non Modifiable factors		
Age (46-55 year)	140	70
Sex	148 (male))	85 (male)
	52 (female	15 (female)
Medical history		
Hypertension	100	50
Chronic kidney disease	32	16
Diabetes mellitus	72	36

Table III. Distribution of patients by clinical presentation (N = 200)

Clinical presentation	Frequency	Percentage
Abdominal pain and Hematuria	44	22
Loin Mass	24	12
Incidental diagnosis	132	66

Table IV. Distribution of patients by clinical evaluation (paraneoplastic Syndrome) (N = 200)

Examination Findings	Frequency	Percentage
ESR	120	60
Hypertension	100	50
Anemia	80	40
Weight loss	26	13
Pyrexia	4	2
Hypercalcemia	4	2

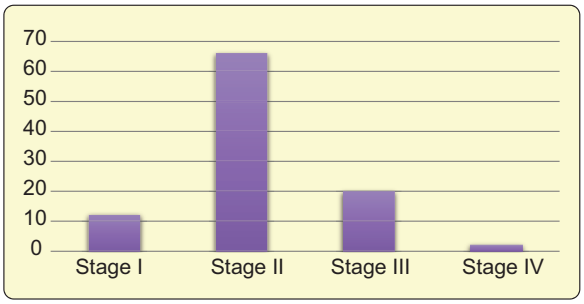

Figure 1. Distribution of the patient by the stage of the disease

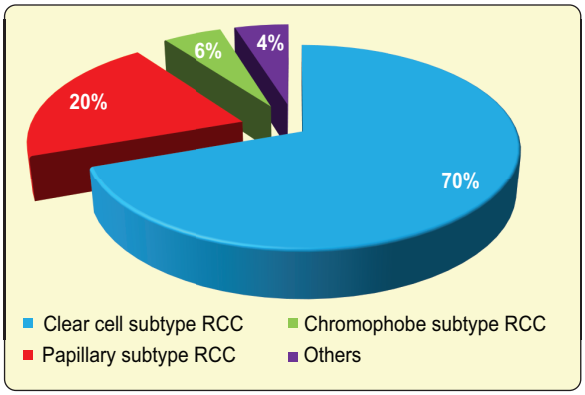

Figure 2. Histopathological diagnosis of 200 cases of renal cell carcinoma

DISCUSSION

The study of RCC included 200 cases treated in BIRDEM during the period of January 2013 to July 2023. All the cases were finally documented by post surgical histo-pathological examination. In our study, we found that most (70%) of patients were between 46-55 year of age group and the median age at diagnosis was 52.28 years and the lowest and the highest ages were 35 and 78 year respectively. Study conducted in Czech Republic[10], Brazil[11] and Columbia University[12] median age at diagnosis was 62, 59.8, 61 year respectively. In our study, median age of presentation was 52.28 year with one-fourth (26.7%) of the patients were less than 50 year of age and 14% below 40 year of age. This shows a much younger age of presentation in this area. These findings are similar to other Indian and Asian studies.[19,20] Asian population has a reportedly low incidence of RCC which may be due to multifactorial including genetic and environ-mental factors or other factors like low reporting.[13] The younger age of presentation may also be attributable to envi-ronmental factors, dietary factors or genetic susceptibility which needs to be addressed by larger epidemio-logical studies.[14] As per existing literature from developed world, the male to female ratio of RCC patients is 2:1.[15] We found higher incidence of renal cancers in males with a male to female ratio of 2.9:1. This finding is similar to that of other Indian studies and Asian countries.[16,17] This may be due to lower incidence of smoking among the women or low socioeconomic conditions leading to difference in treatment seeking behavior.[18] In our study smoking was one of the most common modifiable risk factor, others are excess body weight and alcohol. According to International Agency for Research on Cancer and the United States Department of Health and Human Services, tobacco smoking has been classified as carcinogenic for the kidney.[18.19] In developed countries, it is estimated that 6% of kidney cancer are a result of tobacco smoking[21] which is similar to our study. According to literature high body mass index (BMI) is estimated to be responsible for 26% of incident world wide.[22] But in our study average body weight, lean and thin person were more prone to develop RCC then over weight person. So, body weight is not evident as an important risk factor for development of RCC in our country. As per table II, hypertension, chronic kidney disease and DM were the common associated disease but not proved as paraneoplastic condition. Literature review showed hypertension can predispose to kidney cancer.[23,24] In the United States, a history of hypertension has been estimated to double the risk of kidney cancer in white patients and triple the risk in black patients.[25] Antihypertensive medication has also been associated with an increased risk of kidney cancer but it is difficult to disentangle the effect of the condition from the effect of treatment. Nevertheless, less

documented observation shows, hypertensive condition rather than the treatment, is more likely to be the risk factor. So, controlling hypertension by medication may be an effective therapeutic intervention in the prevention of kidney cancer. Hypertension also seems to be biologically independent from obesity in the risk of kidney cancer and having a cumulative effect among individuals who present with both conditions.[26,27] Although underlying mechanisms are not yet well described, renal injury, hypoxia or inflammation caused by hypertension may play a role.[28,29] Chronic kidney disease increases the risk of kidney cancer two-fold to three-fold.[30,31] The association between DM and kidney cancer have been assessed in several prospective cohort studies with some suggestive evidence of an independent biologic effect from diabetic comorbidities such as obesity and hypertension. Diabetes would be associated with a 40% excess risk of kidney cancer.[34] These findings are similar to that of other global study. In our study, we found that 53% cases of RCC had their lesion in right kidney and 55% cases RCC occurs in upper pole. In a study, Tribhuvan University Teaching Hospital, Kathmandu showed RCC occupying upper pole in 40% of cases. In our study, right RCC is common which is almost similar to the above regional study. The reason why RCC occur in right kidney and upper polar is not yet known. Like many others, we also could not find a reason for upper polar affection. In our study, we found that 67% patients were diagnosed as RCC incidentally, 23% presented with pain and hematuria and 10% present with loin mass. Our study results are similar to international study. It has been established in literature that approximately 20% of patients with RCC develop paraneoplastic syndrome.[32,33] These data have predominantly been derived from Western population. In our study, raised ESR being the commonest among the paraneoplastic syndrome, others are hypertension, anaemia, thrombocy-tosis, polycythaemia and hypercalcaemia. The postulated mechanisms for paraneoplastic syndrome in RCCs are elevated cytokines (especially IL-6), tumour secreting hepatotoxins and lysozymes (hepatic dysfunction/Stauffer syndrome), renin and IL-6 secretion by tumour cells (hypertension), erythropoietin secretion by tumour cells (polycythaemia), thrombopoietin secretion by tumour cells (thrombocyto-sis), chronic disease, poor nutritional status and increased iron-binding protein lactoferrin (anaemia).[21] Immuno-histochemistry (IHC) is not routinely applied to the tumour slides for demonstration of tumour cell production of the paraneoplastic agent. Interestingly, hypercalcaemia, which has been noted to be a common paraneoplastic syndrome in RCC, was found to be the least common in our study. In our study we found that about 60% RCC size were between 3-7 cm, 30% were more than 7 cm and 10% were less than 3 cm. The size of the tumour appear to be important in the surgical management of the tumour. In Japan, study conducted by Okuda H and others showed in case of RCC where tumour size less than 5 cm, nephron sparing surgery can be done. In the above international study, we have found that, tumour size less than 5 cm has less chance of metastasis and in these cases nephron sparing surgery is possible. In our study, most of the tumour size ranging from 3-7 cm. In our series most of the tumour were large and due to other technical reason less number of patients underwent nephron sparing surgery. In our study, most patients were diagnosed as Robsing Stage II and 20% in stage-I. In one study, conducted in Czech Republic[10], Poprach A, Lakomy R et al Sel, from 2003-2010, out of 544 patients of RCC, diagnosed as stage I in 46.5% cases, stage II in 10.7% cases, stage III in 13.1% cases and stage IV in 20% cases. In West, most of the RCC diagnosed in Robsing stage-I, but in our study most of the RCC were diagnosed in Robsing stage II. In our country due to low socioeconomic and educational ground, our people visit to the doctor later until there is overt complication and that lead to delayed diagnosis. In our study we found that, out of the 200 patients, 140 (70%) cases were diagnosed as clear cell type and 40 (20%) cases were papillary type. In studies conducted in Czech Republic[10], India[34] and Nepal[36] clear cell sub type RCC were found 84.6% , 74.8%, 86% cases respectively.

In a review study of Columbia University, showed that men were more likely to have papillary histology than women. Women were more likely to have chromophobe histology.[12] In our study clear cell sub type RCC was two-thirds, which is almost same in other international study.

The present study had number of limitations. The present study was conducted only in one center in Dhaka city which may not represent the whole country. This study comprise to a small sample size, more

representative study can be conducted with large sample size treated in multiple hospitals of the country.

It had been observed that RCC mostly occurred in young male patient at right kidney with fewer symptomatic detection and at an advanced stage. Tobacco smoking were the most common modifiable risk factor.

Authors' contribution: MRH and RS prepared the study design, collected data, prepared the manuscript. RS designed the questioner, reviewed and edited the manuscript. MRK helped in data collection, supervised patient management. MSA performed statistical analysis and interpretation. MRH drafted and edited the research manuscript, complied data and writing. ATMMC supervised this study. All authors read and approve the final version for submission.

Conflict of interest: Nothing to declare.

REFERRENCES

1. Ljungberg B, Campbell SC, Cho HY, Jacqmin D, Lee JE, Weikert S, et al. The epidemiology of renal cell carcinoma. Eur Urol 2011 Oct 1;60(4):615-21.
2 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185countries. CA Cancer J Clin 2022 Nov;68(6):394-424.
3. Ries LA, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg LX, Eisner MP, Horner MJ, Howlader N, Hayat M. SEER cancer statistics review, 1975-2003.
4. Lindblad P. Epidemiology of renal cell carcinoma. Scand J Surg 2004; 93: 88-96.
5. Khandelwal S, Reddy KS. Eliciting a policy response for the rising epidemic of overweight-obesity in India. Obes Rev 2013;14 (Suppl 2):114-25.
6. Agnihotri S, Kumar J, Jain M, Kapoor R, Mandhani A. Renal cell carcinoma in India demonstrates early age of onset and a late stage of presentation. Indian J Med Res 2014;140:624-9.
7. Srivastava A, Mandhani A, Kapoor R, Jain M, Dubey D, Srivastava A, et al. Prognostic factors in patients with renal cell carcinoma: Is TNM (1997) staging relevant in Indiansubpopulation? Indian J Cancer 2004; 41:99-103.
8. Amin MB, Edge SB, editors. AJCC cancer staging manual. New York; Springer: 2017.
9. Lopez-Beltran A, Scarpelli M, Montironi R, Kirkali Z. 2004 WHO classification of the renal tumors of the adults. Eur Urol 2006 May 1;49(5):798-805.
10. Poprach A, Lakomy R, Selingerova I, Doleckova B, Nilek O, Hezova R, et al. Epidemiological and clinico-pathological characterstics of patient with renal cell carcinoma: a single institution analysis of 544 cases. Klin Onkol 2013; 16(2): 114-23.
11. Russo P. Renal cell carcinoma: presentation, staging, and surgical treatment. Semin Oncol 2000; 27:160-76.
12. Pierorazio PM, Murphy AM, Benson MC, McKiernan JM. Gender discrepancies in the diagnosis of renal cortical tumours. World J Urol. 2007 Mar;25(1):81-5.
13. Znaor A, Lortet-Tieulent J, Laversanne M, Jemal A, Bray F. International variations and trends in renal cell carcinoma inci-dence and mortality. Eur Urol 2015 Mar 1;67(3):519-30.
14. Lipworth L, Tarone RE, McLaughlin JK. The epidemiology of renal cell carcinoma. J Urol 2006 Dec;176(6):2353-8.
15. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin 2020 Jan;70(1):7-30.
16. Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, Ramchandani P. Campbell-Walsh urology tenth edition.
17. Pang C, Guan Y, Li H, Chen W, Zhu G. Urologic cancer in China. Japanese J Clin Oncol 2016 Jun 1;46(6):497-501.
18. Goggins WB, Wong G. Cancer among Asian Indians/ Pakistanis living in the United States: Low incidence and generally above average survival. Cancer Causes Control 2009 Jul 1; 20(5):635-43.
19. Lushniak BD, Samet JM, Pechacek TF, Norman LA, Taylor PA. The health consequences of smoking—50 years of progress: A report of the surgeon general.
20. Palapattu GS, Kristo B, Rajfer J. Paraneoplastic syndromes in urologic malignancy: The many faces of renal cell carcinoma. Rev Urol 2002; 4(4):163.
21. Dy GW, Gore JL, Forouzanfar MH, Naghavi M, Fitzmaurice C. Global burden of urologic cancers, 1990–2013. European urology. 2017 Mar 1;71(3):437-46.22.
22. Arnold M, Pandeya N, Byrnes G, Renehan AG, Stevens GA, Ezzati M, Ferlay J, Miranda JJ, Romieu I, Dikshit R, Forman D. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. The lancet oncology. 2015 Jan 1;16(1):36-46
23. McLaughlin JK, Lipworth L, Tarone RE. Epidemiologic aspects of renal cell carcinoma. Semin Oncol 2006; 33:527-33.
24. Chow WH, Dong LM, Devesa SS. Epidemiology and risk factors for kidney cancer. Nat Rev Urol 2010; 7:245-57.
25. Colt JS, Schwartz K, Graubard BI, Davis F, Ruterbusch J, DiGaetano R, Purdue M, Rothman N, Wacholder S, Chow WH. Hypertension and risk of renal cell carcinoma among white and black Americans. Epidemiology. 2011 Nov 1;22(6):797-804.

26. Weikert S, Boeing H, Pischon T, Weikert C, Olsen A, Tjonneland A, Overvad K, Becker N, Linseisen J, Trichopoulou A, Mountokalakis T. Blood pressure and risk of renal cell carcinoma in the European prospective investigation into cancer and nutrition. American journal of epidemiology. 2008 Feb 15;167(4):438-46.

27. Chow WH, Gridley G, Fraumeni Jr JF, Järvholm B. Obesity, hypertension, and the risk of kidney cancer in men. New England Journal of Medicine. 2000 Nov 2;343(18):1305-11.

28. Palm F, Nordquist L. Renal oxidative stress, oxygenation, and hypertension. Am J Physiol Regul Integr Comp Physiol 2011; 301:R1229-R1241.

29. Mennuni S, Rubattu S, Pierelli G, Tocci G, Fofi C, Volpe M. Hypertension and kidneys: unraveling complex molecular mechanisms underlying hypertensive renal damage. Journal of human hypertension. 2014 Feb;28(2):74-9.

30. Shebl FM, Warren JL, Eggers PW, Engels EA. Cancer risk among elderly persons with end-stage renal disease: a population-based case–control study. BMC nephrology. 2012 Dec;13:1-8.

31. Hofmann JN, Corley DA, Zhao WK, Colt JS, Shuch B, Chow WH, Purdue MP. Chronic kidney disease and risk of renal cell carcinoma: differences by race. Epidemiology. 2015 Jan 1;26(1):59-67.

32. Gu L, Li H, Gao Y, Ma X, Chen L, Li X, Zhang Y, Fan Y, Zhang X. The association of platelet count with clinicopathological significance and prognosis in renal cell carcinoma: a systematic review and meta-analysis. PloS one. 2015 May 8;10(5):e0125538.

33. Tokuda N, Naito S, Matsuzaki O, Nagashima Y, Ozono S, Igarashi T, Japanese Society of Renal Cancer. Collecting duct (Bellini duct) renal cell carcinoma: a nationwide survey in Japan. The Journal of urology. 2006 Jul 1;176(1): 40-3.

34. Larsson SC, Wolk A. Diabetes mellitus and incidence of kidney cancer: A meta-analysis of cohort studies. Diabetologia 2011; 54:1013-8.

35. Pradhan D, Kakkar N, Bal A, Singh SK, Joshi K. Sub-typing of renal cell tumours; contribution of ancillary techniques. Diagnostic Pathology. 2009 Dec;4:1-8.

36. Sidharth M, Luitel BR, Gupta DK, Maskey P, Chalise PR, Sharma UK, Gyawali PR, Shrestha GK, Sayami G, Joshi BR. Pattern of Renal Cell Carcinoma–A Single Center Experience in Nepal. Kathmandu University Medical Journal. 2011;9(3):185-8.