RESEARCH ARTICLE

Diabetes Mellitus and Renal Cell Carcinoma - A Hospital Based Study from Kathmandu Valley

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Abstract

Objective: To diagnose renal cell carcinoma at early stages and for better prognosis , the main objective of our current study was to understand any association with diabetes with relation to age, gender, history of disease, diabetic laboratory parameters, tumor size and grade. Materials and Methods: This hospital based study was carried out using data retrieved from the register maintained in the Department of Biochemistry of Nepalese Army Institute of Health Sciences between 1st December, 2011 and 31st May, 2012. The variables collected were age, gender, HbA1c, serum creatinine, fasting blood glucose. One way ANOVA was applied to examine statistical significance of differences between groups. The LSD post hoc test was used for the comparison of means of case groups. Results: Of the total 140 cases of renal cell carcinoma, 79 patients were also suffering from diabetes mellitus. The number of females (47) was more in diabetic RCC patients when compared to males (32). Significance was observed in levels of serum creatinine for tumor size >10cm (0.0001*). The highest value of glycated hemoglobin (8.9%) and fasting blood sugar(148.3mg/dl)in cases of renal cell carcinoma along with diabetes mellitus was found in tumour size of 1-5cm. Conclusion: Diabetes mellitus has independent prognostic significance in RCC in relation to tumour size and grade.

Keywords: Diabetes mellitus - renal cell carcinoma - tumour size - grade- Kathmandu

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Introduction

Renal cell carcinoma is the most frequent renal malignancy in adults which grow from the proximal renal tubular epithelium and leads to mortality over 100,000 per year worldwide. In the United States renal cell carcinoma accounts for 2.3% of all cancer deaths. (Jemal et al., 2007). The augmentation of renal cell carcinoma has been reported in most of countries due to change in prevalence of risk factors for RCC. The increase occurrence of RCC have been implicated with cigarette smoking, physical activity, genetic susceptibility, alcohol consumption, occupational exposure to trichloroethylene, obesity, hypertension, kidney transplantation, exposure to certain toxins and family history of the diabetes (Luke et al., 2011). A prior history of diabetes increased the relative risk of cancer by 40% in both men and women. diabetes mellitus as a potential risk factor for renal cell carcinoma has been illustrated in clinical and autopsy findings. Obesity and hypertension are the most important recognized risk factors for renal cell carcinoma and both factors are allied to diabetes mellitus through insulin resistance and metabolic syndrome (Mori et al., 2000). numerous other mechanisms implicated in the development of renal cancer in diabetes include increased growth factors and/or their receptors, hyperinsulinemia and glucose availability. In spite of increased health care services for imaging, still up to one third of all patients with RCC will have metastases at time of presentation (Singam et al., 2010). In the developing countries like Nepal, incidence of diabetes mellitus is very high. To diagnose the renal cell carcinoma at early stages and for better prognosis, the main objective of our current study was to understand the association between renal cell cancer and diabetes with relation to age, gender, history of diabetes, diabetic laboratory parameters, tumor size and grade.

Materials and Methods

It was a hospital based study carried out using data retrieved from the register maintained in the Department of Biochemistry of Nepalese Army Institute of Health Sciences, Nepal between 1st December, 2011 and 31st May, 2012. The variables collected were age, gender, HbA1c, serum creatinine, fasting blood glucose. The glycated haemoglobin was determined by ion exchange chromatography (Eckerbom et al., 1994). Estimation of serum creatinine was done by Jaffe's alkaline picrate method (Peake et al., 2006). The assessment of fasting

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blood glucose was done by glucose oxidase and peroxidase method (Trinder et al., 1969). All these laboratory parameters were analyzed using Human reagent kits and with the help of semi autoanalyser (Humalyser 3500, Germany). Preceding the study, approval for the study was obtained from the institutional research ethical committee. Analysis was done using descriptive statistics and testing of hypothesis. The data was analyzed using Excel 2003, R 2.8.0, Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and the EPI Info 3.5.1 Windows Version. The One way ANOVA was used to examine the statistical significant difference between groups. Post Hoc test LSD used for the comparison of means of case groups. A p-value of <0.05 (two-tailed) was used to establish statistical significance.

Results

Of the total 140 cases of renal cell carcinoma, 79 patients were also suffering from diabetes mellitus.

Table 1 illustrates that number of males (38) were more in cases of renal cell carcinoma when compared to females (23). The maximum number of cases suffering from RCC fall in category of 61-70 years of age. In contrast to that, number of females (47) were more in diabetic RCC patients when compared to males (32). The maximum number of cases suffering from RCC along with diabetes mellitus fall in category of 71-80 years of age.

Table 1. Distribution of RCC and RCC+diabetic subjects according to age and gender

	RCC			RCC+diabetics		
Age	Male	Female	Total	Male	Female	Total
31-40	3	1	4	2	4	6
41-50	2	1	3	3	5	8
51-60	10	6	16	4	7	11
61-70	13	9	22	9	14	23
71-80	10	6	16	14	17	31
Total	38	23	61	32	47	79

Table 2 shows that maximum number of patients suffering from renal cell carcinoma were having the size from 1-5 cm. The mean values of serum creatinine was higher in cases of renal cell carcinoma along with diabetes mellitus when compared to cases of renal cell carcinoma in all the sizes of tumor. The significant changes was observed in levels of serum creatinine in tumor size >10 cm (0.0001*). The mean values of glycated haemoglobin and fasting blood sugar were significantly higher in cases of renal cell carcinoma along with diabetes mellitus when compared to RCC patients (0.0001*). The highest value of glycated hemoglobin (8.9%) and fasting blood sugar (148.3 mg/dl) in cases of renal cell carcinoma along with diabetes mellitus was found in tumor size of 1-5 cm.

Table 3 depicts that the maximum number of patients were suffering from Grade I of renal cell carcinoma (85). The maximum value of glycated haemoglobin in cases of renal cell carcinoma were found in tumor grade II (6.0±1.1%). The maximum value of glycated haemoglobin in cases of diabetic renal cell carcinoma was found in tumor grade IV (9.5±1.9%). The highest level of serum creatinine was found in tumor grade II both in cases of renal cell carcinoma (1.2±0.2 mg/dl) and diabetic renal cell carcinoma (1.6±0.3mg/dl). FBS was maximum elevated in tumor grade IV (95.3±4.2 mg/dl) in patients of renal cell carcinoma and in contrast to that FBS was maximum elevated in tumor grade I (148.1± 8.4 mg/dl) in patients of diabetic renal cell carcinoma.

Discussion

This is the first description to exemplify RCC cases in association with diabetes mellitus in a Nepali population with reverence to age, gender, laboratory parameter and tumor morphology. Our data point towards that there was high occurrence of RCC in cases of renal cell carcinoma along with diabetes in comparison to renal cell carcinoma cases alone. At our institution, we observed that RCC was more in males in RCC cases in comparison to RCC with

Table 2. Comparison of Parameters in Different Sizes of Renal Cell Carcinoma

Tumor size	RCC vs RCC+diabetics					
(N)	HbA1C(%)	p Value	Creatinine(mg/dl)	p Value	FBS(mg/dl)	p Value
1-5 cm (82)	5.9±1.2 vs 8.9±0.8 (5.37, 6.59) (8.58, 9.38)	0.0001*	1.2±0.2 vs1.3±0.1 (1.09,1.30) (1.20,1.40)	0.134	86.5±1.7 vs 148.3±16.8 (78.86, 96.65) (140.00, 156.78)	0.0001*
>5-10 cm (40)	5.2±0.6 vs 7.9±1.3 (4.91, 5.54) (7.27, 8.58)	0.0001*	1.1±0.2 vs 1.3±0.3 (0.98,1.22) (1.22,1.56)	0.005*	93.1±13.9 vs 143.1±20.1 (86.22, 100.10) (133.11, 153.11)	0.0001*
>10 cm (18)	4.8±1.1 vs 7.2±1.4 (4.24, 5.41) (6.53, 7.96)	0.0001*	0.9±0.1 vs1.2±0.1 (0.81,0.98) (1.17,1.32)	0.0001*	90.4±10.3 vs 133.7±11.5 (85.32, 95.56) (120.02, 139.53)	0.0001*

Table 3: Comparison of Parameters in Various Stages of Renal Cell Carcinoma

Tumor grade	RCC vs RCC+diabetics					
	HbA1C%	p Value	Creatinine (mg/dl)	p Value	FBS (mg/dl)	p Value
I (85)	5.4±0.7 vs 8.5±1.1 (5.03, 5.84) (7.91, 9.21)	0.0001*	1.1±0.1 vs 1.4±0.3 (0.99, 1.17) (1.24, 1.64)	0.0002*	86.1±8.6 vs 148.1±8.4 (81.32, 90.94) (143.46, 150.28)	0.0001*
II (10)	6.0±1.1 vs 8.9±1.0 (5.40, 6.71) (8.40, 9.51)	0.0001*	1.2±0.2 vs 1.6±0.3 (1.07, 1.30) (1.40, 1.75)	0.0001*	93.2 ±5.2 vs 141.0±15.1 (90.13, 96.08) (132.55, 149.45)	0.0001*
III (30)	4.5±0.6 vs 7.7±1.0 (4.18, 4.93) (7.11, 8.28)	0.0001*	0.8±0.1 vs 1.5 ±0.1 (0.76, 0.90) (1.40, 1.59)	0.0001*	86.3±3.4 vs 134.2±7.5 (84.44, 88.22) (130.01, 138.39)	0.0001*
IV (15)	5.6 ±1.1 vs 9.5±1.9 (5.04, 6.34) (8.45, 10.64)	0.0001*	0.9±0.2 vs 1.4±0.1 (0.80, 1.07) (1.33, 1.50)	0.0001*	95.3±4.2 vs 147.3±18.8 (92.97, 97.68) (137.07, 157.80)	0.0001*

diabetes. In distinction to that, number of females were more than males in cases of RCC with diabetes when compared to RCC cases. The result specify that the gender distribution of diabetic RCC was different from its non diabetic counterpart, portentous that there may also be disparity in the biology of RCC with diabetic patients. Our findings concurred with the findings with Habib et al. (2012). HbA1C values were significantly higher in patients with tumors 1-5 cm (8.9±0.8) when compared to tumor size of >5-10 cm (7.9±1.3) and >10 cm (7.2±1.4) in diabetic RCC, suggesting that HbA1C may provide a useful marker for early detection of silent or small RCC before they manifest clinically. Fasting boold sugar or serum creatinine levels did not show much noteworthy dissimilarity for tumor size. Our results showed that the frequency of RCC was significantly higher in diabetics (79) when compared to non diabetic counterpart (61). In diabetic patients, pathogenetic mechanisms involved were raised growth factors increased endogenous estrogen levels, end-stage renal disease due to diabetic nephropathy, prolonged exposure to pro-insulin products with some homology to IGF-1, (Lindblad et al., 1999). The other possible biochemical mechanisms were chronic tissue hypoxia, insulin resistance a compensatory hyperinsulinemia, altered endocrine milieu , production of adipokines, hormone replacement therapy, obesity-induced inflammatory response, lipid peroxidation and oxidative stress (Klinghoffer et al., 2009). In relation to tumor staging, our results did not show any significant differences in glycated hemoglobin, serum creatinine and fasting blood sugar. However, tumor staging in adult RCC was a strong prognostic indicator and the presence of in DM patients suggests a favorable response to therapy and survival as there can be increased incidental detection of lower-stage tumors of RCC through the ultrasound and CT.

In conclusion, diabetes mellitus has an independent prognostic significance in RCC in relation to tumor size and grade.

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