RESEARCH COMMUNICATION

Serum Amyloid A as an Independent Prognostic Factor for Renal Cell Carcinoma - A Hospital Based Study from the Western Region of Nepal

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Abstract

Objective: The objective of our present study was to assess the role of serum amyloid A (SAA) in stages and prognosis of renal cell carcinoma. Material and Methods: It was a hospital based retrospective study carried out in the Department of Medicine and Biochemistry of Manipal Teaching Hospital, Pokhara, Nepal between 1st January 2008 and 31st December 2011. The variables collected were SAA, CRP. Approval for the study was obtained from the institutional research ethical committee. Quantitative analysis of human SAA and C-reactive protein (CRP) was performed by radial immune diffusion (RID) assay for all cases. Results: Of the 422 total cases of renal cell carcinoma, 218 patients had normal and 204 abnormal SAA. SAA levels were grossly elevated in T3 stage (122.3 ± SD35.7) when compared to the mean for the T2 stage (84.2 ± SD24.4) (p value: 0.0001). Similarly, SAA levels were grossly elevated in M1 stage (190.0 ± SD12.7) when compared to the M0 stage (160.9±SD24.8) (p: 0.0001). There was no significant association with elevated CRP levels (209.1 ± SD22.7, normal 199.0 ± SD19.5) . Conclusion: The validity of SAA in serum as being of independent prognostic significance in RCC was demonstrated with higher levels in advanced stage disease.

Keywords: Serum amyloid A - renal cell carcinoma - prognostic factor - Nepal

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Introduction

Renal cell carcinoma (RCC), the most frequent type of kidney cancer, is generally increasing across in the world because of the high tendency of having diverse risk factors such as smoking, obesity, dialysis, infection of hepatitis C, metastasis from testicular or cervical cancer and hypertension (Mohan et al., 2009). Kidney cancer accounts for about 2% of the entire cancers and the utmost incident rate is found in Northern America and the lowest incident rates in Asian and African countries. Luke C et al. reported augment occurrence of renal cell carcinoma in Australia with higher incidence in males when compared to females (Luke et al., 2011).

RCC is characterized by an erratic clinical course and has the propensity to recur and metastasize even a number of years after surgery (Singam et al., 2010). Numerous investigators give you an idea about that the extent of tumour spread at the time of diagnosis was concurrent with survival. Different studies illustrate that the levels of serum soluble CD95, soluble interleukin IL-6 and IL-2R as a predictive indicator for renal cell carcinoma. (Kimura et al., 2001). Stimulation of incongruent inflammatory associated cytokines such as IL-1, IL-6 and tissue necrosis factor induce the production of serum amyloid A (SAA) from the various tissues. In the same way, different inflammatory conditions such as infection, trauma or presence of malignancy may cause the rise of SAA which is most likely derived from the liver cells (Kisilevsky et al., 2012). Elevated level of SAA was found to be allied with the various forms of cancers with shortened survival. Though the extensive study has not been done to see the association between SAA concentration and renal cell carcinoma, some findings suggest that evaluation of SAA level in patients with RCC may be a useful prognostic indicator (Fischer et al., 2012). To the best of our knowledge, association of SAA and renal cell carcinoma has not been reported in Nepalese population so for. Thus the main objective of our undertaken study was to assess the role of SAA in prognosis of renal cell carcinoma and to show an association between the level of SAA and stages of renal cell carcinoma.

Materials and Methods

It was a hospital based retrospective study carried out in the Department of Medicine and Biochemistry of Manipal Teaching Hospital, Pokhara, Nepal between

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1st January 2008 and 31st December 2011. The variables collected were SAA, CRP. Approval for the study was obtained from the institutional research ethical committee. Quantitative Analysis of Human serum amyloid A protein (SAA) and C-reactive protein (CRP) was performed by radial immune diffusion (RID) assay for all cases (Chambers et al., 1983). Analysis was done using descriptive statistics and Confidence Interval (CI). 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.

Results

Of the 422 total cases of renal cell carcinoma, 218 patients had normal SAA and 204 patients had abnormal SAA.

Table 1 illustrates that number of patients were divided according to their classification of renal cell carcinoma and CRP levels with normal and elevated SAA levels. The maximum number of patients having normal SAA belongs to T2 stage (36) of RCC. The maximum number of patients having elevated SAA belongs to M0 stage (32) of RCC. 59 patients were having normal serum CRP and SAA. Further, 35 patients of RCC were having elevated serum CRP and SAA.

Table 2 depicts that there was significant difference in between normal and elevated SAA levels in pathological classification and with respect to CRP levels. The maximum mean value in normal SAA levels was observed in M0 stage (5.6±SD1.2) of RCC. The maximum mean value in elevated SAA levels was observed in other subtypes (203.9±SD20.9) of pathological classification. The mean values of SAA were noticeably raised in elevated CRP levels (209.1±SD22.7) and was statistically significant (p value: 0.0001).

Table 3 shows that SAA levels were grossly elevated in T3 stage (122.3 ± SD35.7) when compared to the mean values of SAA in T2 stage (84.2 ± SD24.4) and were statistically significant (p value: 0.0001). Similarly, SAA levels were grossly elevated in M1 stage (190.0 ± SD12.7) when compared to the mean values of SAA in M0 stage (160.9±SD24.8) and was statistically significant (p value: 0.0001). The mean value of SAA depicts slight difference in Grade1 (192.1 ± SD12.5) and Grade2 (200.0 ± SD20.1) of histological classification and found to be statistically insignificant on comparison to each other (p value: 0.199). The mean value of SAA was almost same in clear cell type and other types of histological classification and found to be statistically insignificant on comparison to each other. The mean value of SAA was high in elevated CRP levels (209.1 ± SD22.7) when compared to normal CRP levels (199.0 ± SD19.5) but found to be statistically insignificant on comparison to each other (p value: 0.177).

Table 1. Serum SAA Levels in Cases of Renal Cell Carcinoma in Relation to Pathologic Factors and CRP Levels

Factor	Normal SAA	Elevated SAA
T2	36	30
T3	10	12
M0	37	32
M1	5	12
Grade 1	18	16
Grade 2	14	18
Clear cell subtype	27	20
Other subtypes	6	17
Normal CRP	59	12
Elevated CRP	6	35
Total	218	204

Table 2. Mean Values of SAA in Cases of Renal Cell Carcinoma in Relation to Pathological Factors and CRP Levels.

Factor	Mean values of		p Value
	normal SAA	elevated SAA	
T2	5.2±1.4	84.2 ±24.4	0.0001*
T3	5.3±1.7	122.3±35.7	0.0001*
M0	5.6±1.2	160.9±24.8	0.0001*
M1	4.5±1.2	190.0±12.7	0.0001*
Grade 1	5.3±1.5	192.1±12.5	0.0001*
Grade 2	5.5±1.2	200.0±20.1	0.0001*
Clear cell subtype	5.3±1.4	198.0±18.6	0.0001*
Other subtypes	4.6±1.0	203.9±20.9	0.0001*
Normal CRP	5.6±1.1	199.0±19.5	0.0001*
Elevated CRP	4.6±1.0	209.1±22.7	0.0001*

Table 3. Comparison of Cases of Elevated SAA Levels in Relation to Pathologic Factors and CRP Levels

Variable	Mean values± Standard Deviation (Confidence interval)		p Value
T classification: T2 vs T3			0.0001*
	84.21±24.49 (74.89,93.52)	vs 122.38±35.77 (100.77,144.00)	
M classification: M0 vs M1			0.0001*
	160.94±24.89 (151.80 , 170.07	vs 190.08±12.71 (182.00,198.16)	
Histologic grade: Grade 1 vs Grade 2			0.199
	192.13±12.56 (185.17,199.09)	vs 200.00±20.17 (189.97,210.03)	
Cell Subtype: Clear vs other subtypes			0.383
	198.00± 18.69 (188.99,207.01)	vs 203.94±20.98 (192.75,215.12)	
CRP level: Normal vs elevated			0.177
	199.00±19.50 (186.61,211.39)	vs 209.15± 22.79 (201.20,217.10)	

Discussion

Numerous promising markers for renal cell cancer have been acknowledged; presently not any biomarkers have been authenticated and are in routine use (Eichelberg et al., 2009). This study demonstrated the utility of SAA as potential prognostic serum biomarker. In our current study, prognostic significance was evaluated by TNM staging system that includes tumour grade and histological subtype. There was noteworthy disparity between the values of normal SAA and abnormal SAA for all pathological factors and CRP levels; p Value

(0.0001*). This study examined only T,M, grade, clear cell type in patients of renal cell carcinoma for the independent association of SAA. The faction equated for T classification illustrated the noticeable difference in levels of SAA in T3 stage (122.38±35.77) when compared to T2 stage (84.21±24.49); p Value (0.0001*). In the same way, the groups associated with M classification demonstrate the clear variation in level of SAA in M1 stage (190.08±12.7) when match up to M0 stage (160.9±24.89); p Value (0.0001*). Our results concurred with the findings of Wood SL et al (Wood et al., 2010). In contrast to that, the groups compared for Grade classification confirm the mild difference in levels of SAA in G2 (200.00±20.17) as compared to G1 (192.13±12.56); p Value (0.199). Likewise, in our present study, results indicate that there was insignificant difference for groups equated for cell classification; p Value (0.383). SAA has been documented as acute-phase reactant whose level in the blood is elevated to 1000-fold as part of the body's responses to various injuries, including trauma, infection, inflammation, and neoplasia. Functions of SAA describing to tumourigenesis (Malle et al., 2009) by attaching to extracellular matrix components with consequent potential modification of cell binding, augmentation of plasminogen activation and triggering of matrix metalloproteinase (MMP) production, and was accounted in numerous cell forms including renal cancer cell lines (Paret et al., 2010). Another inflammatory acute phase protein is CRP. It is also increased in tumour, infections and inflammation (Johnson et al., 2012). Serum C-reactive protein has been reported as a prognostic biomarkers in localized and metastatic renal cell carcinoma (Johnson et al., 2011). SAA values were mildly raised in elevated CRP (209.15± 22.79) when compared to normal CRP levels (199.00±19.50) and it was statistically insignificant; p Value (0.177). These findings warrant further study in larger patient groups to determine conclusively the prognostic value of SAA and CRP in combination.

In conclusion, validity of SAA in serum as an independent prognostic significance in RCC was demonstrated with higher levels in advanced stage disease.

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