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ORIGINAL ARTICLE

Comparison of Serum Chromogranin-A with Albumin-Creatinine Ratio among different groups of Type-2 Diabetics

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ABSTRACT

Background: Diabetic nephropathy is a common complication of diabetesmellitus that cause high morbidity & mortality.
Aim: To compare levels of serum chromogranin-A among different groups of type-2 diabetes mellitus patients based on urinary Albumin-Creatinine Ratio.
Study design: Cross sectional comparative.
Methodology: Present study was conducted at Chemical Pathology Department of General Hospital-Lahore. Patients (n=116) were enrolled through probability convenient sampling. Urine samples were centrifuged to obtain clear supernatant. In this separated supernatant urinary albumin and creatinine was measuredBlood samples were segregated accordingto the study groups (A, B, C and D). Serum was separated for analysis of serum creatinine and serum chromogranin A by ELIZA method. Data was evaluated by using SPSS v.24. ANOVA was used to compare mean levels of urinary ACR AND serum CgA amongthe groups with P-value of 0.05 was considered as significant.
Results: The results showed that serum Chromogranin-A level was high in diabetic patients with normalACR and kept on rising with increasing ACR. Data of age was normally distributed whereas, the distribution of albumin creatinine ratio and serum chromogranin-A was not normal.
Conclusion: It was concluded that serum Chromogranin A can be used as early marker for the diagnosis of diabetic nephropathy thus can help in better management of nephropathy due to diabetes.
Keywords: Diabetic Nephropathy, Albumin-Creatinine Ratio, Serum Chromogranin-A and Type-2 Diabetes.

INTRODUCTION

Diabetic nephropathy (DN) is one of the most common complication of diabetes mellitus and is associated with increased morbidity & mortality. Many different routes and mediators plays a part in the pathogenesis of a disease, making the process veryintricate and multifactorial. Microalbuminuria [urinary albumin to creatinine ratio (ACR) 30-300 mg/g] is a reliable indicator of early- stage diabetic kidney damage[1]. Many novel biomarkers are being studied as potential replacements for or complements to already utilized biomarkers for the early identification of DN.

Diabetes mellitus is a metabolic condition that is persistent and is characterizedby hyperglycemia. It is possible that this is due to decreased insulin production, resistance to the peripheral effects of insulin, or both of these factors working together.Chronic state of hyperglycemia, in conjunction with the other metabolic abnormalities that occur in individuals with diabetes mellitus, can cause damage to various organ systems, which can result in the progression of disabling and fatal health issues[2].

Serum chromogranin A (CgA), is one such marker and belongs to granin family.Like other low molecular proteins it is also driven by kidneys. Serum chromogranin A is excreted mainly through kidneys so when renal function declines, it is retained in serum causing an increase in its level[3].

The quantity of serum chromogranin A (CgA) is measured and is often referred to as a tumor marker test due to the fact that people who have tumors of the neuro-endocrine system tends to have CgA greater than the normal[4].

Serum chromogranin A is excreted mainly through kidneys so when renal function declines, it is retained in serum causing an increase in its level[5]. In patients with hypertensive ESRD, it is noted that genetic diversity at *CgA* determined disease risk or susceptibility.[67] It is also found that endothelin-1 (EDN1) and CgA secretion has some association. CgA increases the secretion of EDN1 which plays an important part in the pathogenesis of renal disease.

As there is a high incidence in diabetic nephropathy among our population and there is lack of local data that specifically addresses this health issue thus current study was planned. The

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amount of CgA that is excreted through the kidneys increases with a loss in renal function because diabetic nephropathy, the most prevalent consequence of diabetes mellitus, causes renal function to decline.

This study was conducted to measure serum CgA levels based on urinary Albumin-Creatinine Ratio and establish the significance of CgA as a biomarker in the onset and development of DN.

METHODOLOGY

It was a cross sectional comparative study conducted at Chemical Pathology Department of General Hospital-Lahore after approval from ethical committee of Lahore General Hospital. Patients (n=116) were enrolled through probability convenient sampling. Diabetics were divided into normoalbuminuric (group-A), microalbuminuric (group-B) and macroalbuminuric (group-C). Healthy individuals worked as control (group-D). Urine samples were centrifuged to obtain clear supernatant. In this separated supernatant urinary albumin and creatinine was measured and ACR calculated in Group A, B, C and D. Blood Samples were segregated according to the study groups (A, B, C and D). Serum was separated from blood in gel tube for analysis of serum creatinine by colourimetric method kits on fully automated spectrophotometer and serum chromogranin A by ELIZA method. Informed consent was taken. Patients of either gender who had type 2 DM > 1 year and confirmed by standard diagnostic tests as per WHO criteria were included. Patients on insulin therapy, having co-morbidities like hypertension, malignancy and any endocrine disorder were excluded.

Statistical analysis: Data was evaluated by using SPSS v.24. ANOVA was used to compare mean levels of urinary ACR AND serum CgA amongthe groups with P-value of 0.05 was considered as significant. Shapiro-wilk test was used to assess the normality of quantitative variables.

RESULTS

Data of age was normally distributed whereas, the distribution of albumin creatinine ratio and serum chromogranin-A was not normal as summarized in table-1.

General parameters like age and serum albumin creatinine ratio among different groups of enrolled participants were summarized as Mean±SD in table-2. There was significant difference between groups for ACR and serum Chromogranin-A levels while insignificant difference for age among participants.

No significant difference was found in gender distribution among the groups as shown by figure 1.

Group D's average albumin creatinine ratio was considerably lower than that of other groups (A, B and C). The average albumin creatinine ratio showed a significant difference between the A, B, and C groups (Table-3).

The post hoc Mann Whitney test was employed for multiple comparisons, and it revealed that group D's average serum Chromogranin-A levels were considerably lower than those of the other groups (A, B and C). In addition, group C's serum Chromogranin A level was much higher than that of groups A and B's. The mean serum Chromogranin A levels between the A and B groups also differed significantly (Table-4).

Table 1:

Variables	Groups	Shapiro-Wilk		
		Statistic	N	p-value
Age (years)	A	0.955	29	0.242
	B	0.950	29	0.185
	C	0.956	29	0.259
	D	0.934	29	0.072
Albumin Creatinine Ratio (ACR)	A	0.873	29	0.002
	B	0.904	29	0.012
	C	0.949	29	0.177
	D	0.893	29	0.007
Serum Chromogranin A (ng/ml)	A	0.953	29	0.220
	B	0.965	29	0.441
	C	0.544	29	0.102
	D	0.854	29	0.001

Table-2: Age, ACR and Serum Chromogranin-A distribution among participants

Parameters	Mean ± SD				P-value
	Group-A	Group-B	Group-C	Group-D	
Age (years)	46.3 ± 13.1	47.3 ± 8.2	49.1 ± 8.1	42.8 ± 16.5	0.250
ACR (mg/g)	9.5 ± 0.6	80.7 ± 30.6	503.1 ± 127.1	4.8 ± 0.2	< 0.001*
Serum CgA	4.1 ± 0.7	5.6 ± 0.4	7.1 ± 0.7	2.0 ± 0.1	< 0.001*

*Statistically Significant

Figure 1: Distribution of gender among groups.

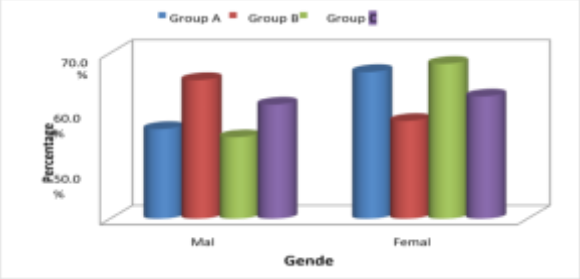

Table-3: Pair wise comparison of mean ACR among study groups.

Groups	Groups	Mean Difference	p-value
A	B	-71.20*	0.006*
	C	-493.53*	< 0.001*
	D	4.7489*	0.006*
B	C	-422.33*	0.006*
	D	75.95*	< 0.001*
C	D	498.28*	< 0.001*

*Statistically significant

Table-4: Pair Wise Comparison of Mean Serum CgA among Groups

Groups	Groups	Mean Difference	p-value
A	B	-1.538*	0.007*
	C	-3.036*	<0.001*
	D	2.100*	0.005*
B	C	-1.499*	0.008*
	D	3.638*	<0.001*
C	D	5.136*	<0.001*

*Statistically significant

DISCUSSION

Diabetes type 2 is the primary cause of end-stage renal disease (ESRD), where as diabetic nephropathy (DN) is thought to be responsible for almost half of all cases of ESRD.[8] To predict the onset and progression of DN clinically, albuminuria is the most commonly used marker. However, traditional DN markers are neither sensitive nor specific enough to detect early stages of DN. Furthermore, glomerular filtration rate (GFR) and albuminuria are not strongly related.[9] Therefore it is vital to find a marker that is more reliable & can help in earlier diagnosis and intervention of DN so that the permanent damage caused by DN can beprevented.

In table-2, mean age of the patients in the groups A, B, C and D was not statistically different. One previous study had mean ages in the four groups i.e. Normoalbuminuria, Microalbuminuria, Macroalbuminuria & controls were higher than the ages in the groups of our current study[10]. They showed late onset of diabetes mellitus and DN. The difference in the ages in this Chinese DM population and present study subject in which DN started to appear might be explained due to variable environmental factors that include better diet, exercise routines and less stressfulenvironment[11].

In present study out of 87 patients of T2 DM 38 were males i.e., 45% and 49 were females i.e., 55%. In a study on diabetic nephropathy, there were 58% male diabetic patients while 42% were females. This difference in the gender for diabetic prevalence may be due to various genetic factors including genetic variations making females more prone to DM[12].

The current study showed that macroalbuminuria was more prevalent in femaleswhereas microalbuminuria was more prevalent in males i.e 68.5 % of females had macroalbuminuria (Group C) and 58.6% of males had microalbuminuria (Group B). A study on DN showed that 53.21% male and 40.3% females were normoalbuminuric[13]. This difference might be explained due to good compliance, more active life style and good dietary habits among their population.

Mean levels of serum chromogranin A, showed that diabetics have higher levels than controls with highest level in macroalbuminuric group. A study measured CgA levels in T2DM patients which were significantly high than the healthy individuals. Our study also showed the association of CgA with the diabetic progression[14].

Limitations of study: This study was conducted only on a small size of population, therefore to generalize the results for larger groups, the study should be performed on a larger scale. Financial constrains and limited resources with no genetic workup and long follow-ups added to limitations.

CONCLUSIONS

It was concluded that serum Chromogranin A level was high in diabetic patients with normal ACR and kept on risingwith increasing ACR. Therefore, CgA can be used as early marker for the diagnosis of diabetic nephropathy thus can help in better management of nephropathy due to diabetes.

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