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ORIGINAL ARTICLE

Correlation of Serum Chromogranin A with HbA1c and eGFR in Different Groups of Type 2 Diabetic patients

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ABSTRACT

Background: World health organization estimated that around 422 million people are living with diabetes and there is an increasing trend in the numberof diabetic patients.
Aim: To correlate the levels of serum chromogranin A with HbA1c and eGFR in differentgroups of type 2 diabetic patients based on urinary Albumin- Creatinine Ratio.
Methodology: This cross sectional comparative study was done by enrolling 116 patients at Chemical Pathology Department, LGH-Lahore through probability convenient sampling. Urine samples of all subjects were centrifuged in-order to measure urinary albumin and creatinineLaboratory parameters like Urinary albumin, Serum creatinine and HbA1c were measured. HbA1c was measured using HPLC method**.** Serum creatinine was measured kits on fully automated spectrophotometer. Abbreviated MDRD equation calculated eGFR. Data SPSS v.24 analyzed the data. ANOVA test applied with P-value of less than 0.05 was considered significant. Spearman correlation was also applied to correlate HbA1c and eGFR with CgA in each group.
Results: The results showed that eGFR was normally distributed whereas, the distribution of albumin creatinine ratio, HbA1c, serum creatinine and serum chromogranin-A were not normal. Between the A, B, and C groups, no discernible variationin the mean HbA1c values was found.
Practical Implication: Due to lack of literature review and high incidence of diabetes induced nephropathy in our setups, there is need to find a parameter than can correlate nephropathy among diabetics.
Conclusion: It was concluded that early diagnosis of diabetic nephro-pathy can be evaluated by using serum Chromogranin-A but it has a negative correlation with eGFR and positive correlation with HbA1c.
Keywords: Diabetic Nephropathy, HbA1c, Estimated Glomerular Filtration Rate, Serum Chromogranin-A and Type-2 Diabetes.

INTRODUCTION

Diabetes mellitus is a global health challenge. W.H.O estimated that around 422million people are living with diabetes and that there is a increasing trend in the numberof diabetic patients. According to a Survey the prevalence of diabetes in Pakistan is 26.3%[1]. Diabetic nephropathy (DN) being most common and seriouscomplication of diabetes mellitus (DM) is associated with raised morbidity and mortality rate in diabetic patients[2]. In China, cases of DN have also raised drastically over last ten years. According to one estimate, CKD among Chinese diabetics reached 24.3 million[3] however, similarly higher prevalence kidney functional impairment among Pakistani newly diagnosed diabetic was 24.4%[4].

Diabetes mellitus is a metabolic disorder characterized by persistently high glucose levels in blood and low or absent serum insulin due to impaired functioning of β-pancreatic cells.[5] Chronic hyperglycemia results in various complications like electrolyte imbalance followed by organ damage. Commonly, it affects kidney, eyes and neurons thus ending in permanent organ damage[2,5].

Main source of serum chromogranin-A is kidneys so its amount in serum is dependent on renal function. Once the renal function deteriorates than its serum levels drop dramatically[3]. Chromogranin A is produced by the endocrine and neuroendocrine cells of a variety of organs. The amount of chromogranin A in the serum is most often used in the diagnosis of neuroendocrine tumours as well. According to the research that has been done so far, chromogranin A is one of the factors that plays a part in the development of diabetes mellitus[5,6].

Identification and monitoring of DN primarily involve 2 diagnostic methods: assessment of renal function in terms of estimated glomerular filtration rate (eGFR) and estimation of renal damage with regard to Albumin to Creatinine Ratio ACR[7]. The pathophysiology of numerous renal disorders includes the involvement of tub.

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International studies showed that CgA can be an important diagnostic marker of diabetes progression but unfortunately, lack of local data and high rate of diabetes among our population regarding its role made us conduct present study. Thus correlation between levels of serum chromogranin-A with HbA1c and eGFR in different groups of type 2 diabetic patients based on urinary Albumin- Creatinine Ratio was done.

The objective of the study was to correlate the levels of serum chromogranin A with HbA1c and eGFR in differentgroups of type 2 diabetic patients based on urinary Albumin- Creatinine Ratio.

METHODOLOGY

Present cross sectional comparative study was done by enrolling 116 patients at Chemical Pathology Department, LGH-Lahore through probability convenient sampling. Urine samples of all subjects were centrifuged in-order to measure urinary albumin and creatinine.Diabetics were divided into normoalbuminuric (group-A), microalbuminuric (group-B) and macroalbuminuric (group-C). Healthy individuals worked as control (group-D). After taking an informed consent from the study subjects, all the concerned information such as gender, age, and disease duration were taken on a pre-designed proforma. EDTA blood was used for HbA1c measurement in each group. Laboratory parameters like Urinary albumin, Serum creatinine and HbA1c were measured. HbA1c was measured using HPLC method**.** Serum creatinine was measured kits on fully automated spectrophotometer. Serum Chromogranin A was measured by using ELISA technique. Abbreviated MDRD equation calculated eGFR[10]. Diabetic patients (> 1year) of either gender were included while those having complications as well as secondary health issues while on insulin therapy were excluded.
Statistical analysis: Data SPSS v.24 analyzed the data. ANOVA test applied with P-value of less than 0.05 was considered significant. Spearman correlation was also applied to correlate HbA1c and eGFR with CgA in each group. Shapiro-wilk test was used to assess the normality of quantitative variables.

RESULTS

Results revealed that eGFR was normally distributed while remaining parameters were not normal as summarized in table-1. Insignificant difference was seen for gender distribution among all groups as given in table-2.

General parameters like HbA1c, serum Chromogranin-A levels, serum creatinine and serum albumin creatinine ratio showed significant difference among all groups p-value of less than 0.05 summarized in terms of Mean **±** SD (Table-3)

No significant difference was found in gender distribution among the group. Results revealed that group D's average HbA1c was considerably lower than that of the other groups overall (A, B and C) as shown in Table-4

Between the A, B, and C groups, no discernible variation in the mean HbA1c values was found. Results showed that group B and C's average eGFR was considerably lower than group A and D's. Additionally, group C's eGFR was much lower than group B's. However, there was no discernible difference in mean eGFR between the A and D groups as shown in Table-5.

Data were not distributed in a typical way. In order to ascertain the relationship between urinary albumin-creatinine ratio, eGFR, and serum Chromogranin A in study participants, the Spearman Rho correlation test was utilised. The results revealed that serum Chromogranin A had significant strong positive correlation with HbA1c and urinary albumin-creatinine ratio while negative correlation with eGFR in all diabetic patients (groups A, B and C). In healthy controls serum Chromogranin A had no significant correlation with eGFR and urinary albumin- creatinine ratio while serum Chromogranin A had significant positive correlation with HbA1c as shown in table-6.

Table-1: Normality of quantitative variables

Variables	Groups	Shapiro-Wilk		
		Statistic	N	p-value
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*
HbA1c	A	0.890	29	0.006*
	B	0.925	29	0.041*
	C	0.935	29	0.072
	D	0.885	29	0.004*
Serum Creatinine	A	0.904	29	0.013*
	B	0.901	29	0.011*
	C	0.927	29	0.047*
	D	0.954	29	0.226
eGFR (ml/min/1.73m^2)	A	0.929	29	0.052*
	B	0.980	29	0.850
	C	0.965	29	0.440
	D	0.943	29	0.122

*Statistically significant

Table-2: Subjects distribution in terms of gender among groups

Gender	Groups			
	A	B	C	D
Male	11(37.9%)	17(58.6%)	10(34.5%)	14(48.3%)
Female	18(62.1%)	12(41.4%)	19(65.5%)	15(51.7%)

P value 0.242

Table-3: HbA1c, ACR and Serum Distribution among ParticipantsChromogranin-A

Parameters	Mean ± SD				P-value
	Group-A	Group-B	Group-C	Group-D	
HbA1c	9.3 ± 0.6	9.8 ± 1.7	9.8 ± 2.2	5.9 ± 0.3	< 0.001*
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*
Serum Creatinine	0.74 ± 0.08	0.94 ± 0.22	1.02 ± 0.20	0.83 ± 0.13	< 0.001*
eGFR	102.0 ± 18.8	81.3 ± 18.4	70.6 ± 14.0	99.0 ± 8.1	< 0.001*

*Statistically Significant

Table-4: Pair wise comparison of mean HbA1c among study groups

Groups	Groups	Mean Difference	p-value
A	B	-0.566	> 0.999
	C	-0.497	> 0.999
	D	3.344*	< 0.001*
B	C	0.0690	> 0.999
	D	3.910*	< 0.001*
C	D	3.841*	< 0.001*

*Statistically significant

Table-5: Pair wise comparison of mean eGFR among study groups

Groups	Groups	Mean Difference	P value
A	B	20.64*	< 0.001*
	C	31.42*	< 0.001*
	D	3.021	0.878
B	C	10.78*	0.044
	D	-17.62*	< 0.001*
C	D	-28.40*	< 0.001*

*****Statistically significant

Table-6: Correlation of serum Chromogranin A with HbA1c, eGFR and urinaryalbumin-creatinine ratio

Group	Serum Chromogranin A	HbA1c	eGFR	Urinary albumin-creatinine ratio
Diabetic (n=87)	Spearman RhoCorrelation	0.213	-0.563	0.872
	p-value	0.047*	<0.001*	< 0.001*
Health controls (n=29)	Spearman RhoCorrelation	-0.377	0.041	0.061
	p-value	0.044*	0.834	0.754
All study participants (n=116)	Spearman RhoCorrelation	0.647	-0.626	0.931
	p-value	< 0.001*	< 0.001*	< 0.001*

*Statistically significant

Correlation between serum Chromogranin-A and HbA1c among participants.

DISCUSSION

Unfortunately, traditional serum markers like albuminuria and glomerular filtration rate areneither sensitive nor specific enough to detect early stages of diabetic nephropathy[11,12]. Therefore, need of hour is to find a reliable serum marker for early detection of DN in-order to prevent permanent damage caused by diabetes.

Mean HbA1c % levels (Table- 4) showed that there was no statistically difference among diabetic groups A, B & C which shows lack of control of diabetes. One previous study showed that there was no statistically difference in HbA1c among diabetic groups based on ACR. This finding was consistent with results of present study[13].

One previous study showed that CgA levels were significantly higher in among diabetic patients in comparison to healthy individuals. Similarly, our results showed that high levels of CgA were associated with progression of disease among our diabetic patients[14].

Mean SCR levels (Table-1) showed that SCR increases with increase in ACR & with progression of diabetic nephropathy whereas mean levels of eGFR (Table-5) showed a significant decrease in eGFR levels in microalbuminuric & macroalbuminuric groups with increase in ACR & progression of diabetic nephropathy. Similarly, one previous study showed that mean SCR levels among diabetics increased with rise in ACR while

mean levels of eGFR decreased respectively thus depicted that their levels with disease progression leading to nephropathy[15].

Our results revealed that serum Chromogranin-A had significant strong positive correlation with HbA1c and urinary albumin-creatinine ratio while negative correlation with eGFR in all diabetic patients. Similarly, one previous study showed that serum Chromogranin-A had insignificant correlation with eGFR in all diabetic patients. According to them, it cannot be used as early marker for diabetic nephropathy[16].

According to one previous study, serum CgA levels were higher in patients with T2DM than in control subjects, and a statistically significant difference among the studied subgroups regarding CgA was found ($P < 0.05$). The levels of serum CgA increased gradually with the degree of DN ($P < 0.001$). Serum CgA levels showed a moderate-intensity positive correlation with UACRs ($P < 0.001$). A cutoff level of 3.46 ng/ml CgA showed 69.86% sensitivity and 66.12% specificity to detect DN in the early stage.[17] Their results were in line with our findings that showed higher serum CgA levels with deteriorating renal functions.

Limitations of study: Financial constrains, small sample size and limited resources with no genetic workup added to our limitations.

CONCLUSIONS

It was concluded that early diagnosis of diabetic nephro-pathy can be evaluated by using serum Chromogranin-A but it has a negative correlation with eGFR and positive correlation with HbA1c.

Author's contribution: AG, HH &NK: Overall supervision and Write up and literature review. **IN, AA &SSK:** Literature review help in write-up.

Running head: Relationship between Serum Chromogranin-A with disease progression and control.

Conflict of interest: None

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