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SERUM INFLAMMATORY MARKERS OF DIABETIC KIDNEY DISEASE AND THEIR CORRELATION TO LIPID PARAMETERS AMONG DIABETIC INDIVIDUALS OF EASTERN INDIA

Biochemistry

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ABSTRACT

Background : Diabetes mellitus is the leading cause of chronic renal failure . As the period of diabetes progresses there is simultaneous increase of inflammatory markers like high sensitive C reactive protein (hsCRP) with degree of renal involvement, suggested by albumin creatinine ratio and also dyslipidemia in diabetic patients.

Materials & Methods: 120 diabetic individuals aged (30-60) yrs, divided in 3 groups of 40 subjects in each, namely: a) newly diagnosed<5 years b) 5-10 years after diagnosis and c) ≥10 years after diagnosis were recruited as study subjects from a tertiary care hospital in sub Himalayan region.

Results : Descriptive studies showing mean values of hsCRP ,ACR & lipid parameters were done in all 3 groups. One-way ANOVA with post hoc analysis after Bonferroni correction in 3 different groups enunciated a significant and statistical increase ($p < .001$) of both hsCRP &ACR with duration of diabetes unlike the lipid parameters. hsCRP, ACR, cholesterol & LDL even illustrated a very significant correlation between each other ($p<0.001$) , TG to hsCRP while HDL showed no correlation to any parameters.

Conclusion: Early detection, monitoring of inflammatory markers hsCRP, ACR & deranged lipid parameters are predictors of diabetic nephropathy that can help in modulating diabetes and its complications.

KEYWORDS

Diabetes; hsCRP ; ACR; lipid parameters

INTRODUCTION:

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action/ resistance or both. [1]It is the major cause of chronic renal failure.[2,3] and thereby becomes a major public health problem in developed as well as developing countries like India resulting in major morbidity . [4][5] Diabetes cannot be cured; it can only be prevented or managed.

Since kidney failure in diabetic patients leads to mortality 20-40 times likelier than those without DM, prevention & early diagnosis of kidney dysfunction is very important. [6,7] The cost of treatment and its burden of morbidity is imposed on the individual as well as on health system of the country.

The earliest evidence of nephropathy is the appearance of low but abnormal levels of albumin (30-299mg/day) in urine referred to as microalbuminuria. [8] Though the gold standard for measuring urine albumin excretion is by collecting 24 hours urine sample (as per American Diabetic Association).[9] still urinary Albumin (in µg) to creatinine(in mg) ratio (i.e.ACR) provides a more convenient way to measure microalbuminuria on random urine sample, as recommended by the National Kidney Foundation[10]. Urinary albumin–creatinine ratio is now integral to the classification of chronic kidney disease (CKD). It is now recommended that all patients with diabetes and/or hypertension be screened annually with this test.[11]

Serum CRP levels are elevated in response to acute infections, inflammatory conditions and trauma while hsCRP help quantify low grades of systemic inflammation, in the absence of overt systemic inflammatory or immunologic disorder, detectable at a very low range (.03mg/dl). [12] Thus hsCRP accurately identifies low but persistent levels of inflammation. It has been anticipated that hsCRP (marker of inflammation) shows a significant rise along with ACR. [13]The objective of the study was to show simultaneous increase of blood level of hsCRP with degree of renal involvement suggested by ACR in diabetic patients, as the period of diabetes progresses.

MATERIALS AND METHODS :

It was an Institution based observational comparative study conducted in a tertiary care hospital in sub himalayan region from April 2016- March 2017. Sample size was 120 individuals selected through convenient technique from 120 diabetic individuals (approximate) aged (30-60) yrs irrespective of gender, divided in 3 groups of 40 subjects in each, namely: a) a) newly diagnosed<5 years b) 5-10 years after diagnosis and c) ≥10 years after diagnosis have been taken.The sampling was done from our institute which consists of patients residing in sub Himalayan areas with mixed ethnicity.

Based on some prefixed inclusion i.e. diabetic and exclusion criteria like any acute or chronic ailment, pre-diagnosed renal or cardiac pathology, patients on drugs that can modify renal function e.g.- beta- lactam antibiotics, cyclosporine or any drugs that causes hyperglycemia e.g.- thiazides, HRT, OCP etc , pregnancy, endocrinopathies or malignancy ; the study population had been chosen from the known/diagnosed diabetic patients referred to a tertiary care hospital in North Bengal for diabetic profile. Verbal consent was sought from all the subjects. Study was also approved from ethical committee. Approximately 2ml of venous blood was collected from peripheral veins of patients in clotted vials . After separating serum from the blood samples in clotting vials using centrifugation, those were used to estimate serum hsCRP. Random urine sample were used to measure urine micro-albumin and urinary creatinine, to determine ACR .All the samples were measured by semi-automated analyzer or automated analyser.

RESULTS :

Table 1. Descriptive statistical chart of serum hsCRP (mg/dl), urinary albumin creatinine ratio(ACR) and lipid parameters in different study groups

VARIABLES	Mean ± SD		
	Group I (N=40)	Group II (N=40)	Group III (N=40)
hsCRP (mg/dl)	0.04 ± 0.005	0.08 ± 0.011	0.10 ± 0.017
ACR (mg/gm Cr.)	100.29± 11.59	117.65 ± 6.93	128.80 ± 7.9
CHOL (mg/dl)	205 ± 18.36	219.6 ± 17.23	215.04 ± 17.41
TG (mg/dl)	223 ± 15.45	223.9 ± 14.81	191.57 ± 18.80

HDL (mg/dl)	49 ± 11.81	50.05 ± 9.43	50.05 ± 11.18
LDL (mg/dl)	125.7 ± 17	139.31 ± 17.41	135.4 ± 18.21

Mean values of hsCRP were found to be 0.04 ± 0.005, 0.08 ± 0.011, & 0.10 ± 0.017 and that of ACR were 100.29 ± 11.59, 117.65 ± 6.93 & 128.80 ± 7.91 in group 1,2 ,3 respectively

Table 2: ANOVA With Post Hoc Analysis After Bonferroni Correction Of Hscrp ,ACR, Cholesterol ,TG, HDL & LDL Between Different Groups Under Study

	parameters	Significance (p)
Group I vs. Group II	ACR	**<.001***
	hsCRP	**<.001***
	CHOL	.005
	TG	1.00
	HDL	1.00
	LDL	.065
Group II vs. Group III	ACR	**<.001***
	hsCRP	**<.001***
	CHOL	1.00
	TG	.030
	HDL	1.00
	LDL	.293
Group I vs. Group III	ACR	**<.001***
	hsCRP	**<.001***
	CHOL	.036
	TG	.009
	HDL	1.00
	LDL	1.00

One way ANOVA between different groups shows statistical significance at (p<.001)

One-way ANOVA with post hoc analysis after Bonferroni correction between different groups enunciated that both hsCRP & ACR increased significantly and statistically (p <.001) with duration of diabetes in all 3 groups unlike the parameters of lipid profile.

Table 3: Pearson Correlation Coefficient Between HsCRP, ACR and lipid parameters in all 3 study groups taken together

parameters		hsCRP	ACR	CHOL	TG	HDL	LDL
hsCRP	Pearson correlation	1	.851	.281	.195	.076	.267
	Significance (p)		<.001*	.002*	.033*	.411	.003*
ACR	Pearson correlation	.851	1	.229	.139	.033	.278
	Significance (p)	<.001*		.012*	.130	.71	.002*
CHOL	Pearson correlation	.281	.229	1	.114	-.291	.556
	Significance (p)	.002*	.012*		.217	.001*	<.001*
TG	Pearson correlation	.195	.139	.114	1	.140	.021
	Significance (p)	.033	.131	.217		.127	.822
HDL	Pearson correlation	.076	.033	-.291	.140	1	-.012
	Significance (p)	.410	.717	.001*	.127		.900
LDL	Pearson correlation	.267	.278	.556	.021	-.012	1
	Significance (p)	.003*	.002*	<.001*	.822	.900	

Values with (*) in the groups show correlation at the significance level of (p <.001) or (p<.05)

Above table shows a very significant correlation between hsCRP & ACR(p<0.001). Among the lipid parameters, cholesterol & LDL elicited good correlation with hsCRP & ACR and even to each other (p=0.001) .TG was evaluated to have mild correlation to hsCRP while HDL showed no correlations to other parameters.

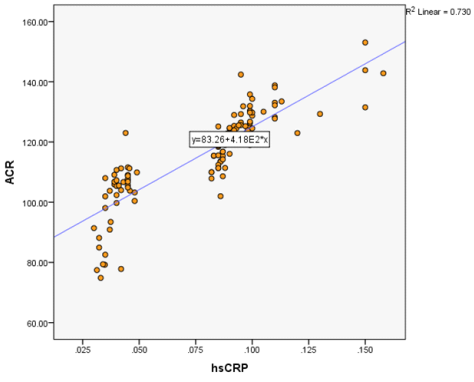

FIG 1 :- Significant correlation between hsCRP and ACR among cases of all 3 Groups.

DISCUSSION:

Microalbuminuria which is considered an early stage of diabetic nephropathy ,is also a predictor of cardiovascular disease in diabetics.[14,15] Microalbuminuria typically occurs after 5 years in diabetes. Overt nephropathy, with urinary protein excretion higher than 300 mg/day, often develops after 10 to 15 years. ESRD develops in 50% of type 1 diabetics, with overt nephropathy within 10 years.In a study conducted by Shin DI et al in the year 2013 [16] it was demonstrated that there is independent association of ACR with hsCRP (r = 0.62, P < 0.001), Thus ACR level was proved to be positively correlated with the hsCRP levels in type 2 diabetic patients.
In the current study an increase in ACR values by 71 in the 1st group, 88 in the 2nd group and by almost 99 in the 3rd group from the reference normal range (i.e 0-29µg/mgU.cr) was depicted. As already stated earlier that >5 yrs is known as the starting point of nephropathy, therefore early detection is important.

Shin DI et al,in a study in the year 2013 [17] demonstrated that there is independent association of ACR with hsCRP (r = 0.62, P < 0.001). ACR level was proved to be positively correlated with the hsCRP levels in type 2 diabetic patients. Our findings are in unison with previous studies on the associations of hsCRP with ACR .

Among the lipid parameters cholesterol & LDL in this study are seen to have good correlation to each other and only meek correlation with hsCRP & ACR (p<.05) . This was in accordance with the previous study reported in 2004 by E.S. Kang et al [18] , in 2009 by M.L Marcovecchio etal.[19] and even demonstrated by Almquist, T.etal in 2014[20]. Further in our study ,triglyceride also showed mild correlation to hsCRP (p<.05) . Thereby hsCRP, ACR is noted to be associated more significantly with each other as compared to lipid parameters.

This study represents a unique example as it can further be extended with appropriate sample size. Thus this can as well serve as a pilot study. Such a duration based study in diabetes has not yet been done in the mixed ethnic population of Eastern India, more to say in sub Himalayan region.

These observations emphasizes that patients with high hsCRP and ACR are at increased risk of diabetic nephropathy. The parameters of lipid profile are non inflammatory, which increase in equal significance with the inflammatory parameters such as hsCRP & ACR. Lipid parameters which are done routinely for diseased patients can help in early detection of micro inflammation & renal pathology in diabetes.Therefore this suggests overall reflection of the disease itself which is revealed by change in renal function.

CONCLUSION:

Early detection, monitoring of inflammatory markers hsCRP, ACR & deranged lipid parameters are predictors of diabetic nephropathy that can help in modulating diabetes and its complications.

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