ORIGINAL ARTICLE

Association of Serum Hs-CRP with Urinary Albumin Creatinine Ratio and Lipid Profile in Diabetic Individuals Attending a Tertiary Care Hospital in the Sub-Himalayan Belt

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Abstract

Aims: The aim of the study was to show a simultaneous increase of high sensitive C-reactive protein (hs-CRP) with a degree of renal involvement suggested by albumin-creatinine ratio and dyslipidemia in diabetic patients, as the period of diabetes progresses. No such duration based study has ever been conducted so far in the sub-Himalayan region and fringe area including different ecosystem as in the present study.

Materials and methods: It was an Institution based observational comparative study conducted in a tertiary care hospital in sub-Himalayan belt from April 2016 to March 2017 among 120 diabetic individuals aged (30–60) years irrespective of gender, divided into 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. Research variables were hs-CRP, urinary ACR and lipid profile.

Results: Descriptive studies showed that mean values of hs-CRP were 0.04 ± 0.005, 0.08 ± 0.011, and 0.10 ± 0.017 and that of ACR were 100.29 ± 11.59, 117.65 ± 6.93 and 128.80 ± 7.91 in groups 1, 2, 3, respectively. One-way analysis of variance (ANOVA) with post hoc analysis after Bonferroni correction between different groups enunciated that both hs-CRP and ACR increased significantly and statistically (p <0.001) with a duration of diabetes in all three groups unlike the parameters of lipid profile. Hs-CRP, ACR, cholesterol and LDL even illustrated a very significant correlation between each other (p <0.001) whereas TG and HDL have shown correlations neither to themselves nor other parameters.

Conclusion: Early detection, monitoring of inflammatory markers hs-CRP and ACR as predictors of diabetic nephropathy can help in modulating diabetes and its complications.

Keywords: ACR, Diabetes, Hs-CRP, Lipid profile.

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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 blindness, kidney failure, heart attacks, stroke, and lower limb amputation,[2] and thereby becomes a major public health problem in developed as well as developing countries like India resulting in major morbidity for an individual in an active period of life.[3,4] 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 and early diagnosis of kidney dysfunction are very important.[5] The cost of treatment and its burden of morbidity is imposed on the individual as well as on the health system of the country.

The earliest evidence of nephropathy is the appearance of low but abnormal levels of albumin (30–300 mg/day) in urine referred to as microalbuminuria.[6] Though the gold standard for measuring urine albumin excretion is by collecting 24 hours urine sample (as per American Diabetic Association).[7] 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.[8] The 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.[9]

Serum CRP levels are elevated in response to acute infections, inflammatory conditions, and trauma while hsCRP help quantifies low grades of systemic inflammation, in the absence of overt systemic inflammatory or immunologic disorder, detectable at a very low range (0.03 mg/dL).[10] Thus hs-CRP accurately identifies low but persistent levels of inflammation.[11] It has been anticipated that hs-CRP (a marker of inflammation) shows a significant rise along with ACR.[12] The objective of the study was to show a simultaneous increase in the blood level of hs-CRP with a degree of renal involvement suggested by ACR in diabetic patients, as the period of diabetes progresses.

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Materials and Methods

It was an Institution based observational comparative study conducted in a tertiary care hospital in the sub-Himalayan region from April 2016 to March 2017. Sample size was 120 individuals selected through convenient technique from 120 diabetic individuals (approximate) aged (30–60 years) irrespective of gender, divided into 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 has 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. The study was also approved from ethical committee. Approximately 2 mL of venous blood was collected from peripheral veins of patients in clotted vials. After separating serum from the blood samples in clotted vials using centrifugation, those were used to estimate serum hs-CRP. A random urine sample was used to measure urine micro-albumin and urinary creatinine, to determine ACR. All the samples were measured by semi-automated analyzer or automated analyzer.

Table 1: Descriptive statistical chart of serum hs-CRP (mg/dL), urinary albumin-creatinine ratio (ACR) in different study groups

	Mean ± SD		
Variables	*Group I (n = 40)*	*Group II (n = 40)*	*Group III (n = 40)*
hs-CRP (mg/dL)	0.04 ± 0.005	0.08 ± 0.011	0.10 ± 0.017
ACR	100.29 ± 11.59	117.65 ± 6.93	128.80 ± 7.9

Note: data above shows mean & SD of hsCRP and ACR in all 3 groups

Table 3: ANOVA with post hoc analysis after bonferroni correction of hs-CRP, acr, cholesterol, tg, HDL and lDL between different groups under study

	Parameters	*Significance (p)*
Group I *vs.* Group II	ACR	<0.001
	hsCRP	<0.001
	CHOL	0.005
	TG	1.00
	HDL	1.00
	LDL	0.065
Group II *vs.* Group III	ACR	<0.001
	hsCRP	<0.001
	CHOL	1.00
	TG	0.030
	HDL	1.00
	LDL	0.293
Group I *vs.* Group III	ACR	<0.001
	hsCRP	<0.001
	CHOL	0.036
	TG	0.009
	HDL	1.00
	LDL	1.00

One way ANOVA between different groups shows statistical significance at (p <0.001)

Results

The mean and standard deviation of concentration of hs-CRP (mg/dL) in newly diagnosed diabetics (<5 years), known diabetics from (5–10 years) and those diagnosed >10 years back were (0.04 ± 0.005), (0.08 ± 0.011) and (0.10 ± 0.017), respectively (Tables 1 to 4).

Discussion

Microalbuminuria which is considered an early stage of diabetic nephropathy is also a predictor of cardiovascular disease in diabetics.[13,14] 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,[15]

Table 2: Descriptive statistical chart of lipid profile parameters in the 3 study groups taken together

	Mean	*Std. Deviation*
CHOL	211.0909	30.27898
TG	227.3256	58.52000
HDL	49.7719	10.81749
LDL	133.5050	26.47001

Note: Data showing mean, S.D of Lipid parameters

Table 4: Pearson correlation coefficient between Hs-CRP, ACR and lipid profile parameters in all 3 of the study groups

Groups	*Correlations of parameters*		*Correlation coefficient (r)*	*Significance (p)*
Group I	hs-CRP	ACR	0.661	<0.001
		CHOL	0.668	<0.001
		TG	0.272	0.090
		HDL	–0.089	0.58
		LDL	0.294	0.065
Group II	hs-CRP	ACR	0.637	<0.001
		CHOL	0.213	0.187
		TG	0.189	0.242
		HDL	0.146	0.367
		LDL	0.359	0.023
Group III	hs-CRP	ACR	0.661	<.001
		CHOL	0.668	<.001
		TG	0.012	0.942
		HDL	0.002	0.989
		LDL	0.588	<0.001

Note: Values in the groups show a correlation at the significance level of (p <0.001)

it was demonstrated that there is an independent association of ACR with hs-CRP (r = 0.62, p <0.001), thus ACR level was proved to be positively correlated with the hs-CRP levels in type 2 diabetic patients.

In the current study, the mean values of hs-CRP were found to be 0.04 ± 0.005, 0.08 ± 0.011, and 0.10 ± 0.017 and that of ACR were 100.29 ± 11.59, 117.65 ± 6.93 and 128.80 ± 7.91 in groups I–III, respectively. This depicted 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., 0–29 µg/mgU.cr). As already stated earlier that >10 years is known as the starting point of nephropathy; therefore early detection is important. One-way ANOVA with post hoc analysis after Bonferroni correction between different groups enunciated that both hs-CRP and ACR increased significantly and statistically (p <0.001) with a duration of diabetes in all three groups unlike the parameters of lipid profile.

Shin DI et al., in a study in the year 2013,[15] demonstrated that there is an 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. Our findings are in unison with previous studies on the associations of hsCRP with ACR in diabetes as in the present study, and we illustrated a very significant correlation between hs-CRP and ACR (*p* <0.001). Among the lipid profile parameters, cholesterol and LDL elicited good correlation with hs-CRP and ACR and even to each other (*p* = 0.001) whereas TG and HDL showed correlations neither to themselves nor to other parameters. Thereby hs-CRP is noted to be associated more significantly with ACR as compared to lipid profile 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 North East India, more to say in the sub-Himalayan region.

These observations emphasize that patients with high hsCRP and ACR are at increased risk of diabetic nephropathy. The parameters of the lipid profile are noninflammatory, which increase in equal significance with the inflammatory parameters such as hs-CRP and ACR. Therefore this suggests an overall reflection of the disease itself which is revealed by a change in renal function.

Conclusion

Early detection, monitoring of inflammatory markers hs-CRP and ACR as predictors of diabetic nephropathy can help in modulating diabetes and its complications.

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