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Original Research Paper

Biochemistry

A DURATION BASED COMPARATIVE STUDY TO CORRELATE hsCRP WITH MICROALBUMINURIA AMONG DIABETIC OUTPATIENTS ATTENDING A TERTIARY CARE HOSPITAL IN SUBHIMALAYAN REGION.

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ABSTRACT

Background: Microalbuminuria in type 2 diabetic patients is speculated to be accompanied by elevated serum high sensitivity C reactive protein (hsCRP). . Establishing a correlation between hsCRP & microalbuminuria relative to duration of diabetes suggests activation of inflammatory pathways in progression of kidney disease .

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 from a tertiary care hospital in sub Himalayan region according to some inclusion and exclusion criteria.

Result: Mean values of hsCRP were 0.04 ± 0.005, 0.08 ± 0.011, & 0.10 ± 0.017 and that of micro albumin were 95.42 ± 12.30, 116.79 ± 4.87 & 130.56 ± 7.65 in group 1,2 ,3 respectively. One way ANOVA with post hoc analysis after Bonferroni correction depicted that both hsCRP & micro albumin increased significantly and statistically with duration of diabetes in all 3 groups along with a very significant correlation between them .

Conclusion: Both serum hsCRP and microalbuminuria increases with period of diabetes.So the increasing trend of these inflammatory markers needs to be noted early and monitored to prevent progression of diabetic nephropathy.

KEYWORDS : Diabetes; hsCRP; Microalbuminuria

INTRODUCTION:

Diabetes is a very fast growing chronic metabolic disorder which has huge social, health and economic consequences. In the recent years, it has become a global epidemic affecting millions of people of all age groups.India, a country experiencing rapid socioeconomic progress and urbanization, carries a considerable share of the global diabetes burden.The complications that are specific to diabetes include retinopathy, nephropathy, and neuropathy. Patients with all forms of diabetes of sufficient duration, including insulin-dependent diabetes mellitus (IDDM) as well as non-insulin-dependent diabetes mellitus (NIDDM), are vulnerable to these complications, which cause grave morbidity. [1,2] Protein glycation and the formation of advanced glycation end products (AGEs) play an important role in the pathogenesis of diabetic complications like retinopathy, nephropathy, neuropathy, cardiomyopathy along with some other diseases such as rheumatoid arthritis, osteoporosis and aging [.3]

CRP is a protein that increases in the blood with inflammation.The hsCRP test accurately measures low levels of C-reactive protein to identify low but persistent levels of inflammation and consequently helps to predict a person's risk of developing CVD. In type2 diabetic patients without insulin treatment, elevated levels of plasma hsCRP have been found associated with insulin resistance/hyperinsulinemia and cardiovascular autonomic dysfunction. [4,5,6]

The term microalbuminuria is defined by a urinary albumin excretion (UAE) higher than normal (≥30 mg/L) but lower than 300 mg/L, the lowest detection limit of proteinuria as measured by standard laboratory methods [7] Increasing albuminuria is a strong predictor of progressive renal dysfunction and heightened cardiovascular risk. [8,9] A significant rise in hsCRP occurs after the onset of microalbuminuria in diabetes.[8,10]The objective of the study was to establish a correlation between hsCRP & microalbuminuria relative to duration of diabetes.

REVIEW OF LITERATURE

Diabetes is an "iceberg" disease; a chronic condition associated with increased morbidity, mortality and health care costs. Although an increase in the prevalence and incidence of type 2 diabetes have occurred globally, they have been especially dramatic in societies in economic transition, in newly industrialized countries and in developing countries. It has been proven in a study in 2013 by Pitocco et al and by Domingueti in 2016 that oxidative stress plays a key role in the pathogenesis of insulin resistance and β-cell dysfunction in type 2 diabetes and its vascular complications, the leading cause of death in diabetic patients.[11,12] Asegaonkar SB. et al in 2011 in a study proved hsCRP, a proinflammatory circulating marker as an independent cardiovascular risk marker among Indians with type 2 diabetes even with normal lipid profile [13]. Microalbuminuria is independently associated with arterial stiffness and vascular inflammation in patients with newly diagnosed type 2 diabetes or essential hypertension, which emphasizes the importance of proactive clinical investigations for atherosclerotic complications in patients with microalbuminuria.[9] M.loredana et al. in an article in 2008 showed that a significant rise in hsCRP occurs after the onset of microalbuminuria in diabetes. In the year 2009, it was evaluated by Mohammad Javed Mojahedi et al that in type 2 diabetes microalbuminuria is accompanied by elevated hsCRP, suggesting activation of inflammatory pathways in progression of renal disease.[8] This finding of microinflammation as a common risk factor for progression of nephropathy & atherosclerosis was also depicted in the Japanese population in 2010.[14] . Finally, in a series of latest studies, namely by Waheed P et al & Najafi L et al in 2016 and by Litikesh AB in 2017 it was demonstrated that hsCRP and microalbuminuria are early markers of diabetic nephropathy.[15,16,17]

MATERIALS AND METHODS

This Institution based observational comparative study was conducted in a tertiary care hospital in the subhimalayan region from April 2016- March 2017.120 individuals were selected through convenient technique from 120 diabetic individuals 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 cause 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 2ml of venous blood was collected from peripheral veins of patients in clotting vials . Random/ spot urine sample was also collected. After separating serum from the blood samples in clot vials using centrifugation, those were used to estimate serum hsCRP. Spot/ random urine sample was processed for microalbumin estimation. Ordinarily all the samples were measured by semi-automated analyzer.

RESULTS AND DISCUSSION

Microalbuminuria is an important entity which denotes an early stage of renal involvement in diabetes It has been anticipated that hsCRP shows a significant rise along with microalbuminuria.[18,19,20].Justification of selecting diabetic population in the study group based on duration of diabetes lies within the fact that as time advances in the disease process, there is progression of renal involvement .Prevention and early diagnosis of kidney dysfunction is very important in this group of patients .[21,22]

Table 1: Descriptive statistical chart of serum hsCRP (mg/dl) and urinary microalbumin in different study groups

VARIABLE	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
Microalbumin (mg/l)	95.42 ±12.30	116.79 ± 4.87	130.56 ± 7.65

Table 2: ANOVA with Post Hoc Analysis after Bonferroni Correction of hsCRP & microalbumin between different groups under study

	Parameters	Significance (p)
Group I vs. Group II	hsCRP	<.001
	µ alb	<.001
Group II vs. GroupIII	hsCRP	<.001
	µ alb	<.001
Group I vs. Group III	hsCRP	<.001
	µ alb	<.001

Descriptive findings in our current study (table1) showed that mean values with standard deviation of hsCRP in newly diagnosed diabetics (<5 yrs) , known diabetics from (5-10yrs) and those diagnosed (>10) yrs back were 0.04 ± 0.005, 0.08 ± 0.011, & 0.10 ± 0.017 and that of micro albumin were 95.42 ± 12.30, 116.79 ± 4.87 & 130.56 ± 7.65 in group 1,2 ,3 respectively

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 in above table depicted that both hsCRP & micro albumin increased significantly and statistically (p <.001) with duration of diabetes in all 3 groups

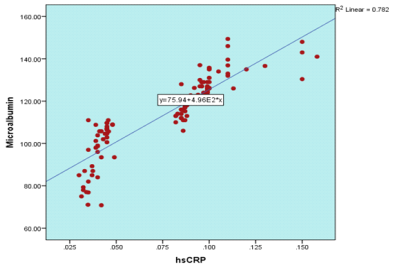
Values in all groups show correlation at the significance level of (p< .001)

Even here a very significant correlation exist between them (p<0.001,i.e. pearsons correlation coefficient = .884).Thus, the result obtained in the current study is in accordance with the findings of the above-mentioned studies.

Table 3: Pearson Correlation between hsCRP and urinary µalb in each Group

Correlation between hsCRP and urinary microalbumin		
GROUPS		
	Pearson correlation coefficient (r)	Significance (p)
Group I	0.686	< .001
Group II	0.672	< .001
Group III	0.657	< .001

FIG 1: Significant correlation between hsCRP and urinary microalbumin level among cases of all 3 Groups.



These observations suggest that low grade inflammation reflected by high serum hsCRP levels plays major role in the induction of microalbuminuria and that irrespective of treatment, inflammation and nephropathy progresses. This study represents a unique example as it can further be extended with appropriate sample size. Nevertheless this can as well serve as a pilot study. Such a duration based study of diabetes has not yet been done in the mixed ethnic population of North East India, more to say in the sub Himalayan region.Consequently, early diagnosis may help to prevent progression of kidney diseases. [23,24,25]

CONCLUSION : Both serum hsCRP and microalbuminuria increases with period of diabetes.So the increasing trend of these inflammatory markers needs to be noted early and accordingly monitored to prevent progression of diabetic nephropathy..

LIMITATIONS

- short period
- small sample size
- Not a longitudinal population based study
- hospital based study

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