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Research Article

RELATIONSHIP OF HS-CRP LEVEL IN DIABETIC PERSONS FREE FROM MICRO AND MACROVASCULAR DISEASE

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ABSTRACT

C-reactive protein is considered as one of the most sensitive markers of systemic inflammation. Studies have found that increase in the levels of C-reactive protein is associated with the vascular complications.

Hence we aimed in finding the correlation of hs-crp with other risk factors like BMI, FBS and HbA1c in diabetic subjects who have still not developed any micro and macrovascular complications. 229 cases of type 2 diabetics and 205 healthy individuals were selected as per the criteria. BMI was calculated, FBS was estimated by glucose-oxidase peroxidase method. Hs-crp was estimated by immunoturbidometric technique. The group was divided into low risk and high risk group as per their hs-crp level. Correlation was seen with other factors like BMI, FBS and HbA1c. The level of Hs-crp was high in diabetic subjects when compared to normal individuals. Further when the diabetic subjects were divided into high risk and low risk groups, the difference between the groups were statistically significant. Hs-crp failed to show any correlation with BMI, FBS and HbA1c. Diabetes is considered as an inflammatory disease hence we observed an increase in the hs-crp level in diabetes than in the normal. Since the vascular complication was totally absent hs-crp failed to show any correlation with BMI, FBS and HbA1c.

Keywords: BMI, Diabetic, Hs-crp, vascular complication.

INTRODUCTION

Diabetes is a metabolic disorder associated with Insulin resistance or insulin action resulting in hyperglycemia. It is considered that hyperglycemia is itself an inflammatory condition. Further classical risk factors like obesity, smoking, hyperlipedemia also exacerbated the condition of inflammation. However inflammatory process is difficult to measure directly. Use of imaging technique or arterial biopsy is not practical. Hence inflammatory biomarkers proved useful information on the inflammatory process. This is a non specific process, any inflammation in other tissue, organs raises the levels of inflammatory biomarkers in the plasma and is associated with the degree of inflammation. Thus a high sensitive method to detect even small variations of these biomarkers in the blood was of choice. Among the several markers of inflammation Hs-CRP is significantly associated with diabetic population. CRP belongs to the pentraxin family and is an acute-phase reactant. It is mostly

produced in the hepatocytes under the regulation of cytokines (1). The most important functions of CRP include binding to various ligands on destructed tissue followed by proliferation of both anti- and proinflammatory effects (2-4). Studies also support that CRP plays an active role in atherosclerosis(5,6). Hyperglycemia is an associated factor to the increase of serum CRP levels, in uncontrolled type-2 diabetic subjects (7). The United Kingdom Prospective Study (UKPDS) in Type 2 diabetes, have clearly shown that intensive control of hyperglycaemia can reduce the emergence and progression of retinopathy, nephropathy and neuropathy (8). Thus our main objective was to evaluate the levels of hs-crp and examine the association of hs-crp level in the diabetic study population who has still not developed any micro and macrovascular complications.

MATERIALS AND METHODS:

This was a cross sectional study of 229 cases of type 2 diabetics and 205 healthy individuals of Dakshina Kannada district. The study population was aged between 30-65 years. Persons with history of type 2 diabetics for at least one year, without any micro and macro vascular complication and on oral or on diet control were selected as the study group. A similar age matched healthy individual was selected as the control group. Criteria for inclusion were –should have been recognized as diabetic for at least one year, should be on oral hypoglycemic drugs or diet control, free from diabetic neuropathy, nephropathy and retinopathy, free from any pre existing cardio vascular disease, non-pregnant in case of females and free from usage of oral contraceptives.

Diabetic nephropathy was ruled out by Microalbuminuria test in spot urine samples. Any value >300mg per liter was repeated again on the next day and if found the same was excluded from the study. Diabetic neuropathy was examined by micro filament test and quantitative sensitive testing. Subjects were excluded if found positive for the neuropathy test. Cardiovascular disease was ruled out by tread mill test. Retinopathy was identified by the fundus examination of the eye by the professionals. Relevant examination was done to establish the inclusion and exclusion criteria. Written informed consent was obtained from the selected subjects. 5 ml of blood in the fasting state was used. FBS was estimated by glucose-oxidase peroxidase method. Hs-crp was done by Thyrocare diagnostic using immunoturbidometric technique. Anthropometric variables like height and weight were measured as per the standard procedure. Measurements of the weight to the nearest 0.1 kg by a weighing machine and height to the nearest of 0.1 cm by an anthropometer rod were done. BMI was calculated as weight (in kg) divided by height in meter square. HbA1c was done by immunoturbidometry technique by thyrocare technologies Limited by fresh sample. The results were analyzed using SPSS 10.0.Students unpaired 'T' test was used to compare between the two groups and Pearson correlation was used to find the correlation between the parameters of the study population. P value <0.01 was taken as the level of significance. Ethical clearance for the study was obtained from Yenepoya University, Mangalore.

Result:

The results of the study are depicted in the following tables.

Table1: Clinical and Biochemical characteristic of the study population

Parameters	Healthy individuals (n=205)	Diabetic individuals (n=229)	P value
Body mass index (kg/m^3)	27.14 ± 3.39	27.62 ± 4.98	0.2487^{NS}
Systolic Blood pressure(mm Hg)	125.43 ± 9.69	123.24 ± 8.41	0.0099**
Diastolic Blood pressure(mm Hg)	91.36 ± 8.27	100.15 ± 6.42	0.0001***
Fasting Blood Glucose (mg/dl)	77.64 ± 13.23	126.50 ± 35.90	0.0001***
HbA1c (%)	6.25 ± 0.85	6.98 ± 1.13	0.0001***
Hs-Crp (mg/dl)	0.13 ± 0.08	0.41 ± 4.77	0.1449

^{Ns}. Not significant, **. Significantly different at $p < 0.05$,***. Significantly different at $p < 0.001$

In table 1 it was seen that all the mean values of the parameters were higher in diabetic than in normal study subjects except for the systolic blood pressure.

Table 2: Clinical and Biochemical characteristic in normal and abnormal hs-crp of the study population

Parameters	Normal hs-crp <0.3 mg/dl (n=180)	Abnormal hs-crp >0.3 mg/dl (n=49)	P value
Body mass index (kg/m^3)	27.89 ± 4.72	27.08 ± 4.58	0.2854^{NS}
Systolic Blood pressure(mm Hg)	121.93 ± 7.09	128.04 ± 10.93	0.0001
Diastolic Blood pressure(mm Hg)	100.06 ± 5.64	100.49 ± 8.76	0.6755^{NS}
Fasting Blood Glucose (mg/dl)	122.38 ± 31.17	141.63 ± 46.90	0.0008**
HbA1c (%)	6.788 ± 1.079	7.696 ± 1.007	0.0001***
Hs-Crp (mg/dl)	0.13 ± 0.07	1.45 ± 5.92	0.0029**

^{ns} Not significant, **. Significantly different at $p < 0.05$, ***. Significantly different at $p < 0.001$

When the study population was divided based on hs-crp value, it was seen that the difference in their mean value varied significantly except for BMI and DBP as shown in the table 2.

Table 3: Pearsons correlation analysis of hs-CRP and other risk variables in total subjects.

Parameters	r	P value
Body mass index (kg/m^3)	.015	NS
Systolic Blood pressure(mm Hg)	.003	NS
Diastolic Blood pressure(mm Hg)	.005	NS
Fasting Blood Glucose (mg/dl)	.023	NS
HbA1c (%)	.074	NS

Ns not significant

Correlation with hs-crp with other risk factors in the diabetic study population though was positive it was not significant as shown in the table 3.

Table 4: hs-CRP values of diabetic study population expressed in percentage.

hs-CRP (mg/dl)	Diabetic			
	Males(n)	Females(n)	Total	%
<0.07	30	13	43	18.77
0.07-0.11 Low risk	23	23	46	20.08
0.12-0.19 Moderate risk	44	14	58	25.36
0.20-0.29 High risk	21	11	32	13.97
> 0.30 Highest risk	38	12	50	21.83

This table shows the classification of the diabetic study population based on their risk as assessed by hs-crp levels.It was seen that approximately 21% the diabetic study population were having highest risk with regard to the hs-crp level as shown in table 4.

DISCUSSION:

Most of the studies have shown that the systolic and diastolic pressure will be higher in diabetic subjects. Studies have also shown that the hypertensive patients have a strong association with diabetes mellitus (9). Moreover as per the 3rd NHANES, 71% of diabetic individuals were found to have hypertension (10). But in our study when the diabetic subjects were grouped according to hs-crp level (>3 and<3) the difference between their mean value in DBP was not significant but significance was observed in SBP. Moreover hs-crp did not show significant correlation with blood pressure. This might be because that hypertension is one of the risk factor associated with inflammation but exacerbated tissue damage that in needed to show any significant correlation has not set in.

Studies have shown that diabetic subjects usually have a higher BMI (11)than compared to their normal counterparts. Further it was seen in that prevalence of overweight and obesity was more among the adult diabetes (12). In our study there was no much variation in their BMI, this is because that our study population had an age group range from 30-65 years of age. Hence this study failed to show any correlation between the groups.

A lot of attention has been focused on blood glucose level since hyperglycemia has shown in the development of complications associated with diabetes. Further hyperglycemia itself is considered as an inflammatory state. In our study there was a significant difference in the mean value of fasting blood glucose and the glycemic index between the hs-crp group and hs-crp failed to show any significant correlation between FBS and HbA1C in diabetic study population.

Studies by Li CZ et al (13) and Rodriguez(14) were able to show a positive correlation within HbA1c and hs-crp. Thus we were able to observe through our result that the relationship of hs-crp with glycemic control was not enough to influence the inflammation hence the subject were free from vascular complication. Our study was able to highlight that diabetes and high BMI are associated with elevated CRP which was also similar in the studies by Barinas et al (15) and (16) Froehlich et al.

CONCLUSION:

The article provides a comprehensive review that hs-crp which is a sensitive marker of inflammation shows no significant correlation with the risk factors in subjects who are diabetic and who are free from any micro and macro vascular complications. This might be because vascular inflammation has still not begun which reflects on hs-crp level. Hence the current studies consider hs-CRP as the best biomarker in assessing the inflammation and also a CVD risk assessor.

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Declaration of interest: All authors declare that they have no conflicts of interest.

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