

Study of HsCRP in Type 2 Diabetes and its Association with Diabetic Retinopathy

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Abstract:

Background: In worldwide, type 2 diabetes prevalence is increasing in the all age group population. This is a major cause for death and various non-fatal complications. In a recent study it is proved that high risk patients with type 2 diabetes mellitus can be reduced by modification of life styles.

Objective: To assess the serum hsCRP levels in patients with type 2 diabetes and to analyse the levels of hsCRP with severity of diabetic retinopathy.

Methods: This cross sectional-Observational study was conducted among patients visiting the OPD/or admitted in Department of General Medicine, KR Hospital, MMCRI Mysore.

Results: Diabetes is one of the leading health issues in the world. Diabetic complications can lead to morbidity and mortality. There are multiple other factors that hasten the progression of diabetic complications. The study showed a correlation of serum hsCRP level with uncontrolled diabetes. It also proved an association between diabetic retinopathy severity with serum hsCRP levels.

Conclusions: The study showed a significant correlation between serum hsCRP and diabetic retinopathy severity

Keywords: hsCRP, Type 2 Diabetes, association, Diabetic Retinopathy.

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Introduction

In india more than 50% of diabetic individuals, are not aware of their diabetic condition. As Asians are having more waist circumference and the waist to hip ratio, they have more chance of having central obesity. Thus these patients are having greater resistance of insulin. In type 2 diabetes mellitus individuals, the development coronary disease is more common. Moreover, these cardiovascular events are more common in diabetic individuals than those without diabetics. C-reactive protein is synthesized in liver. Once tissue damage or inflammation occurs, CRP activates complement classical pathway, as C-reactive protein is a acute phase reactant. C-reactive protein is largely regulated by circulating levels of interleukin-6 predicts coronary heart disease incidence in healthy subjects.[1] After myocardial infarction and stroke, CRP levels rises significantly in the serum.[2] These increase is observed within 6hours of inflammation and the level may be up to 2000 times normal. High sensitive CRP is a measurement of CRP of lower concentration. It is a

quantitative assay of CRP in plasma, and it gives a new method for identification of rupture of plaque in high risk individuals.[3] For the diagnosis of future myocardial infarction and stroke in a healthy men and women, HSCRP plays an important independent predictor. It also has a role in primary prevention of cardiovascular disease.[4, 5] For the development of cardiovascular disease, CRP and glycosylated hemoglobin are having important increased risk factors. HSCRP indicates inflammation and Hb1c indicates hyperglycemia. Both together establishes cardiac risks in individual with atherosclerosis. In diabetic patients, there will be development of macrovascular changes, when there is a poor control of glycemic level. CRP is a significant risk factor for the development of cardiovascular disease. Increase levels of c-reactive protein is also linked in increased risk for development of diabetes in later stages. Hence the study has been taken up to know the relation between the Hb1c and CRP in type 2 diabetes mellitus.

Diabetes mellitus is one of the leading causes of mortality and morbidity owing to its complications, and it adds significant financial burden on both society and the healthcare system. Diabetic retinopathy (DR) is one of the major visual morbidities associated with diabetes that further leads to maculopathy and retinal neovascularization. 1 Patients with untreated diabetes are 25 times more likely to become blind due to DR and macular edema as compared to those without diabetes. 2 Patients with DR may not present any symptoms until very late stage; hence, patients with diabetes need to keep a regular check and screen for ocular diseases.

According to the Union Health Ministry's survey (2015-2019), the incidence of DR was 16.9% while the incidence of sight threatening DR was 3.6%. The exact sequence of events in the pathogenesis of DR is yet to be investigated while some studies propose microvascular occlusion, oxidative stress, inflammation and abnormal metabolic pathways to be critical contributors. [1,3]

Familial influence and genetic predisposition are other associated factors responsible for DR. [4] Inflammation is a prime factor in DR progression; hence, therapeutic approaches like corticosteroids and anti-vascular endothelial growth factor are found effective in slowing the progression of DR.[5,6] It is mainly classified as non-proliferative DR (NPDR) and proliferative DR (PDR) depending upon the presence of neovascularization, which is further subdivided into mild, moderate, and severe stages.

The management of DR is successfully achieved via a combination therapeutic approach, such as glucose monitoring, laser therapy, and vitrectomy. Glycemic control plays an important role in the management of DR; however, despite this, few patients may still develop DR and some may be spared.[7] Hence this study was conducted to assess the serum hsCRP levels in patients with type 2 diabetes and to analyse the levels of hsCRP with severity of diabetic retinopathy.

Materials and Methods

This cross sectional-Observational study was conducted among patients visiting the OPD/or admitted in Department of General Medicine, KR Hospital, MMCRI Mysore. Secondary sources of information including published articles, journals, books and related websites.

Sample size: 100

Inclusion Criteria:

- Age Above 18 years.
- Patients Diagnosed with type 2 diabetes mellitus based on biochemical parameters

Exclusion Criteria:

- Acute Infections
- Pregnant and lactating women
- Acute cardiovascular and cerebrovascular events.
- Patients with chronic inflammatory conditions.

Methods

After taking the institutional ethical clearance for the study purpose of the study will be explained to the patient and attenders. Written informed consent will be taken from the subjects. Relevant history and clinical examination will be done.

Statistical analysis:

Data obtained from the study will be entered in excel sheets and it will be double checked. Data analyzed using SPSS software version 22.0 and it will be presented as descriptive statistics in form of frequency table, figures and graphs.

Association between variables will be done using chi-square test and unpaired t test for qualitative and quantitative variables. Result will be expressed as mean \pm SD. Correlation of parameters is done by Pearson's correlation formula. A p-value of <0.05 is considered statistically significant.

Results

Majority patients were in the age group of 56 to 70 years. Male: female participation was approximately equal

Table 1: Retinopathy grading distribution in the study group

Grading of Diabetic Retinopathy	Frequency	Percentage
No Retinopathy	43	43%
Mild NPDR	16	16%
Moderate NPDR	14	14%
Severe NPDR	16	16%
POR	11	11%

Patients included in the study were more in the group of no retinopathy.

Table 2: Distribution of study subjects in different group

Diabetic Retinopathy Grading	Age—group			Total	p value
	40 to 55	56 to 70	71 and above		
No Retinopathy	26(60.47%)	16(37.21%)	1(2.33%)	43(100%)	0.009
Mid NPDR	6(37.5%)	9(56.25%)	1(6.25%)	16(100%)	
Moderate N POR	3(21.43%)	9(56.25%)	2(14.29%)	14(100%)	
Severe NPDR	4(25%)	11(68.75%)	1(6.25%)	16(100%)	
PDR	0(0%)	9(81.82%)	2(18.18%)	11(100%)	
Total	39(39%)	54 (54%)	7(7%)	100(100%)	

Diabetic Retinopathy Grading	Sex		Total	p value
	Female	Male		
NO retinopathy	2(58.14%)	18(41.86%)	43(100%)	0.534
tund NPDR	9(56.25%)	7(43.75%)	16(100%)	
Moderate NPDR	6(42.86%)	8(57.14%)	14(100%)	
Severe NPDR	6(37.5%)	10(62.5%)	16(100%)	
PDR	7(63.64%)	4(36.36%)	11(100%)	
Total	53(53%)	47(47%)	100(100%)	

HSCRP and FBS correlation

The Pearson correlation coefficient between S. HSCRP & FBS (mg/dl) is 0.777 and it was statistically significant with a p value of <0.01.

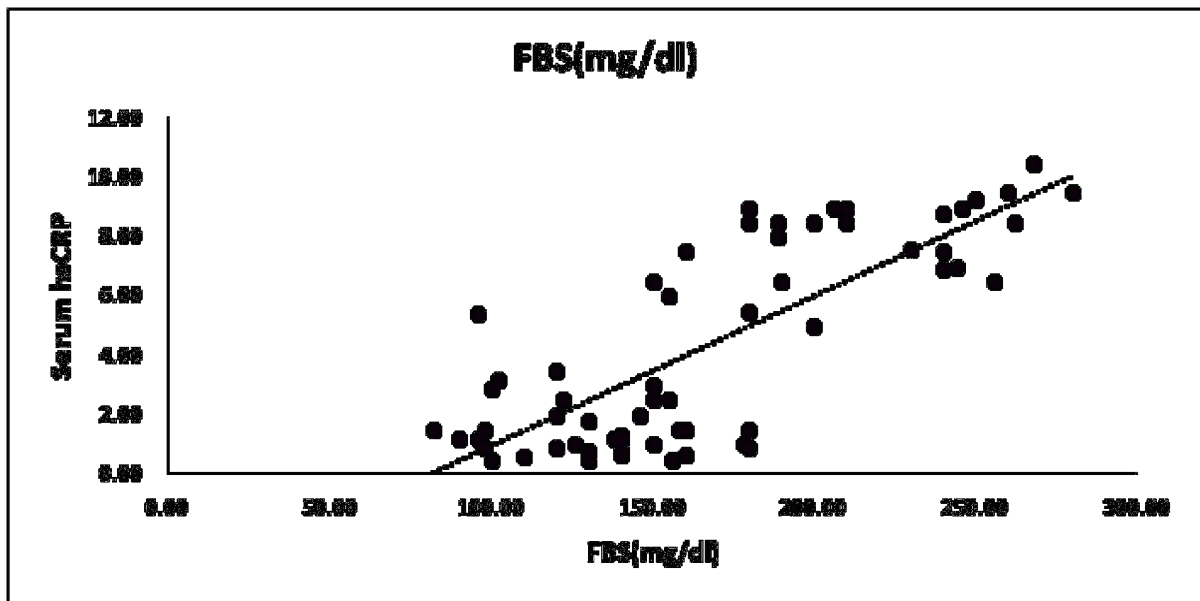


Figure 1:

HSCRP and PPBS correlation

The Pearson correlation coefficient between S. hsCRP & PPBS(mg/dl) is 0.767 and it was statistically significant with a p value of <0.01

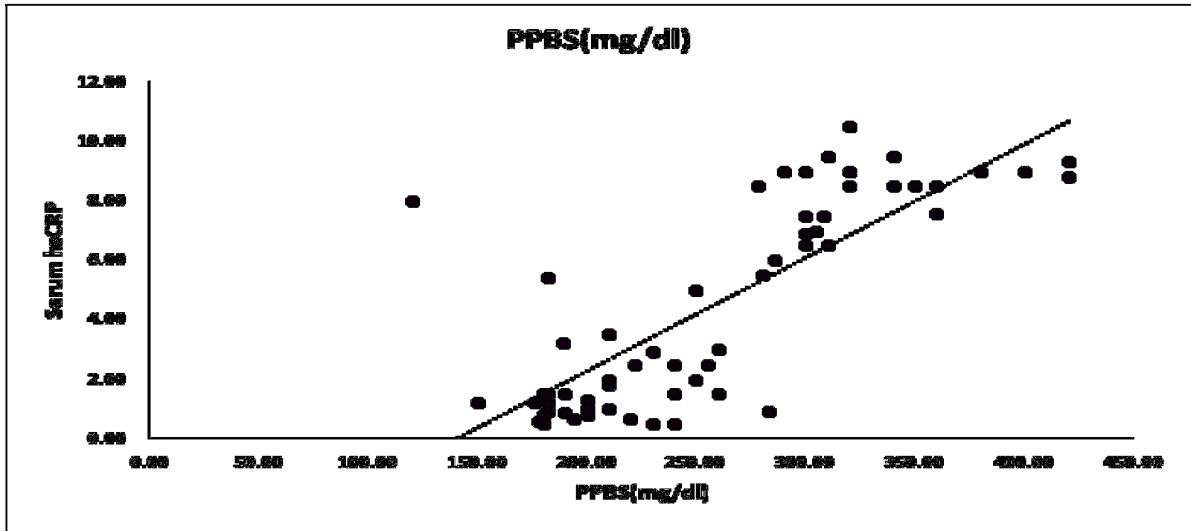


Figure 2:

HSCRP and HbA1c correlation

The Pearson correlation coefficient between S. hsCRP & HbA1c is 0.851 and it was statistically significant with a p value of <0.01

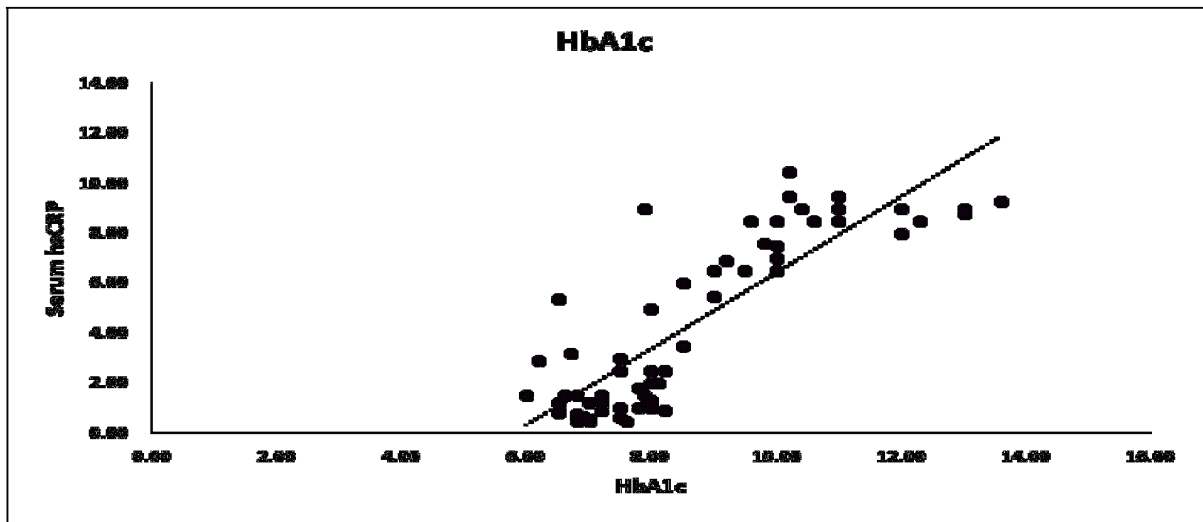


Figure 3:

Table 3: Relationship of duration of diabetes with diabetic retinopathy severity

Diabetic Retinopathy grading	MEAN Duration of diabetes to retinopathy grading	Standard deviation of duration of diabetes to retinopathy grading
No retinopathy	5.69	2.76
Mild NPDR	7.94	1.91
Moderate NPDR	11	2.32
Severe NPDR	13.44	2.16
PDR	18.82	6.16

Diabetic retinopathy severity shows a higher grade with more duration of diabetes. There is association between age and severity of diabetic retinopathy.

Table 4: Relationship of HbA1c with diabetic retinopathy severity

Diabetic retinopathy grading	Mean HbA1c to retinopathy severity	Standard deviation of HbA1c to retinopathy severity
No retinopathy	7	0.51
Mild NPDR	7.99	0.61
Moderate NPDR	9.27	0.84
Severe NPDR	10.24	1.07
PDR	12.19	1.24

Diabetic retinopathy severity was higher in patients with higher HbA1c values. They are associated.

Table 5: Relationship of serum HsCRP to diabetic retinopathy severity

Diabetic Retinopathy Grading	Median hsCRP to severity of retinopathy	Interquartile range
No retinopathy	1	0.7 to 1.5
Mild NPDR	2.5	1.5 to 3.4
Moderate N PDR	6.7	6 to 7.5
Severe NPDR	8.5	7.35 to 9
PDR	9	8.5 to 9.5

Diabetic retinopathy severity showed higher severity in patients with higher values of HsCRP. They are associated. There was a significant association between diabetic retinopathy severity grading and the duration of diabetes, serum hsCRP and serum HbA1c.

Discussion

In the groups studied 53 patients were female and 47 were male. Majority of the patient was in the age group of 56 – 70 years

Table 6:

	Study population	Mean age
Present study	100 cases	61
Study conducted by Manjri Naik and et al[8]	75	62
Study by harishchandra and et al[2]	80	62
Study by sari Marina and et al[1]	51	51

The study conducted by harishchandra et al had a sample size of 80 with the mean age of 62. All other studies had a sample size smaller than the present study.

Among 100 cases, males were 47 and females were 53 with a slight female predominance with female: male ratio of 1.12:1.

Table 7:

	Male to female percentage
Present study	47 male 53 female
Manjri Naik and et al [8]	47 male 28 female
Harishchandra and et al[2]	36 male 44 female
Sari marina and et al, [1]	33 males 18 females

All the studies had a male predominance. The present study had a Male: Female ratio comparable with study conducted by harishchandra et al., The present study focused on serum hsCRP levels in patient who are known case of DM type 2.

The study took random serum hsCRP of all patients as the parameter for comparison. Patient's serum

hsCRP were measured and this parameter was showing a positive correlation with other parameters of diabetes like Duration of Diabetes, FBS, PPBS, HbA1c.

The present study also tried to prove an association between diabetic retinopathy severity with Serum hsCRP levels.

Table 8:

	Investigation Done
Present study	Serum hsCRP
Manjri naik and et al [8]	Serum hsCRP
Harishchandra and et al[2]	Serum hsCRP
Sari marina and et al[1]	Serum hsCRP

The present study was comparing random serum hsCRP value in type 2 DM patients and diabetic retinopathy severity. The present study is comparable with harishchandra et al and manjri naik, both studies compare the same parameter with diabetic retinopathy severity.

The present study was able to prove that there is an HPA axis hyperactivity in uncontrolled diabetic cases and also that cortisol itself can act as a secondary precipitating factor for diabetic microvascular complications like diabetic retinopathy.

Conclusion

The study showed a significant correlation between serum hsCRP and diabetic parameters. It also showed that there is a association between serum hsCRP and diabetic retinopathy severity. Serum hsCRP is a marker of chronic inflammation, precipitating factor for diabetic vascular complication. So screening of serum hsCRP in diabetic will give an idea on overseeing the vascular complications.

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