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Correlation of High-Sensitivity C-Reactive Protein With Blood Sugar Level In Patients With Diabetic Retinopathy

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ABSTRACT
Aim: To study the association of high sensitivity C-reactive protein (hs-CRP) with diabetic retinopathy.

Material and Methods: An observational study was carried out in patients with type 2 diabetes mellitus (DM) both newly diagnosed and known cases of DM admitted in Medicine ward and not suffering from any other inflammatory condition. The hs-CRP levels were measured .Fundus examination was done for grading severity diabetic retinopathy.

Result: Out of 100 type 2 DM patients, 80 patients had retinopathy. 30 patients had mild DR, 40 patients had moderate DR, whereas 8 and 2 patients had severe and very severe diabetic retinopathy high Hs-CRP were found in all cases of diabetic retinopathy and 3 cases with no DR.

Conclusion: The hs-CRP levels were raised in patient with diabetic retinopathy, also hs-CRP levels had association with severity of diabetic retinopathy.
Keywords: High sensitivity c reactive protein , Diabetic retinopathy

I. INTRODUCTION

Diabetic retinopathy (DR), major micro vascular complication of diabetes mellitus (DM), is a major cause of avoidable blindness around the world. Patients with DR are 25 times more likely to become blind than non-diabetics .DR can be divided into non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR)and non proliferative diabetic retinopathy are further divied into mild, moderate , severe and very severe diabetic retinopathy.[1]

- High-sensitivity C-reactive protein (hs-CRP) is an acute phase reactant and a sensitive marker of inflammation. In addition to traditional cardiovascular risk factors, elevation in hs-CRP can be used to predict increased cardiovascular risk in diabetic patients.
- Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. Lack or deficiency of insulin affects the metabolism of carbohydrate, protein, and fat.
- The newer "hs-CRP" is a measure of low-grade chronic inflammation measured by a highly sensitive method. As the name suggests, it is more sensitive than CRP. Hyperglycemia can potentially promote the production of CRP .
- The risk factors (RFs) for DR are divided into two categories: modifiable and non-modifiable . The most significant modifiable RFs include hyperglycemia, hypertension, hyperlipidemia, and obesity. Further modifiable RFs are sleep, prolactin, adiponectin and homocysteine levels, nonalcoholic fatty liver disease, as well as genetic factors, including mutations in the erythropoietin gene promoter. As for the non-modifiable RFs, the most important are DM duration and age of onset, puberty, and pregnancy(3)
- Hyperglycemia, expressed by HbA1c values, is the strongest RF for DR development and progression. Hypertension is another major risk factor.

INFLAMMATION AND DR

- The aforementioned RFs explain only partially the etiology of DR. DM duration, HbA1c levels, hypertension, hyperlipidemia, and the age of DM onset together accounted for only 44,6% and 19,5% of total variances of DR and DME, respectively.[4]
- Therefore many researches investigated other modifiable RFs that could contribute to the disease pathogenesis.
- C-reactive protein (CRP) is mainly produced by the liver and also by atherosclerotic plaques, smooth vascular cells, peripheral leukocytes, adipose tissue, and intra cardial

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tissues. Acute and chronic inflammatory conditions promote the release of IL-6 and other cytokines, which in turn stimulate the hepatic CRP synthesis . CRP is an acute phase and a non-specific inflammatory biomarker, playing a significant role in the innate immunity, the activation of the classical complement pathway, the enhancement of leukocyte reactivity and the production of cytokines.CRP is elevated in several systematic inflammatory conditions, including infections, cancer, rheumatic disease, endothelial dysfunction, obesity and autoimmune diseases. As an inflammatory marker its predictive value is low, whereas its main usefulness is for inflammation screening. High-sensitivity assay for CRP (hs-CRP) detects low (even ≤ 0.3 mg/L) and persistent CRP levels, being thus a significant biomarker of subclinical and chronic inflammation.[3]

- The possible associations of CRP with DR have been studied on a large scale with inconsistent results. Many studies found that DR presence is accompanied by significantly elevated serum CRP and hsCRP levels in both DM types, especially in older patients with longer disease duration, suggesting that CRP ≥3 mg/L could be identified as an independent RF for DR development.[5-7] The novel risk factor like hsCRP is gaining importance as the predictor of vascular events beyond the blood glucose levels. hsCRP levels have been shown to be the markers of atherosclerosis in different studies.[8]Therefore this study aims at assessment of HS-CRP levels and its co relation with severity of diabetes mellitus.

II. MATERIALS AND METHODS

Study design – hospital based study conducted in department of ophthalmology.

100known cases of diabetes mellitus attending opd were selected.Personal information including the age and sex of the patient, duration of diabetes, type of diabetic treatment (diet control only, oral medication or insulin injection), smoking status and presence of hypertension was collected. Blood sample of 3 ml was drawn in the morning following 8 h of fasting under all aseptic precautions for assessment of Hs-CRP.

Inclusion criteria:

1. Patients diagnosed as T2DM on the basis of Clinical history and WHO criteria.
2. Age group between 30 years to 70 years.

Exclusion criteria:

1. Individuals with severe inflammatory diseases, infections , cardiac, hepatic or renal diseases and persons on drugs that would affect blood glucose levels were excluded from the study.
2. Patients with malabsorption or chronic diarrhea.
3. Pregnant and lactating women were excluded from the study.
4. Persons not willing to participate in the study.

All the questions for eliciting history were administered to the patient in his/her own language. Best corrected Snellen's acuity was recorded and slit lamp examination was performed to document any abnormality in the anterior segment. Intraocular pressure was measured using applanationtonometer before dilating the pupils. There was, however, no contraindication for dilatation in any patient. Retinopathy was assessed after adequate mydriasis .Standard techniques and equipment were used for retinal evaluation by using a direct/indirect ophthalmoscope or 90D lens on slit lamp and by fundus photography. A modified version of the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system was used to grade retinopathy.

III. RESULTS

Out of 100 cases evaluated 80 patients were found to have diabetic retinopathy ,patients with diabetic retinopathy were categorized as per ETDRS guidelines as shown in table no.1.patients with high Hs- CRP were categorized into 3 groups as shown in table no.2.All very severe and severe cases had >3mg/dl of Hs-CRP,35 patients having moderate DR and 5 patients of mild DR fell into 1-3mg/dl catogory,25patients of mild DR and 5 patients of moderate DR fell into category of <1mg/dl, 3 patients with no DR also showed <1mg/dl of Hs-CRP levels.

Table :1

Grade of diabetic retinopathy	No. of patients
No DR	20
Mild DR	30
Moderate DR	40
Severe DR	8
Very severe DR	2

Table :2

Hs-CRP levels in mg/dl	No. of patients
<1	35
1-3	35
>3	15

IV. DISCUSSION

- DM is characterized by clustered metabolic abnormalities including hyperglycaemia, elevated triglycerides, low HDL cholesterol, and central obesity. Levels of hs-CRP are significantly elevated in individuals with DM.Dr.manjirnaik et al showed strong association of highly sensitive CRP with diabetic retinopathy in their study conducted at MGM medical college. In the Hoorn study , a large population-based cohort study of 625 adults, higher CRP was associated with the prevalence of any DR(9).our study which is similar to other studies also proves strong association of high levels of Hs-CRP with diabetic retinopathy.
- The limitations of this study are that it is clinic based and the sample size is small. Although referral bias cannot be excluded, this is unlikely to affect our results significantly.
- The strength of this study is that it is based on retinal photography and standard grading techniques and indeed one of the studies which include educating the public about the prevalence and prevention of diabetic retinopathy including its complications.

V. CONCLUSION

Older tests measured CRP levels from 3 to 200mg/l hence in the earlier studies the lower limit of detection was truncated at 3mg/l due to the limits of diagnostic test used. Whereas Hs-CRP measures as low as 0.2mg/dl.Therefore conclusion of this study show string association of Hs-CRP with severity of DR.

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