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Original Research Article

Correlation of C-Reactive Protein levels with severity of Diabetic Retinopathy

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Abstract:

Objectives: The present study was to correlate the C-Reactive Protein levels, BMI and duration of diabetes mellitus with severity of diabetic retinopathy.

Methods: A complete assessment including demographic details, ocular symptoms duration of DM, treatment taken for diabetes, and other associated conditions were performed to all diabetes mellitus patients. Ophthalmic examination included visual acuity, best corrected visual acuity, slit lamp examination for anterior segment were performed. Dilated fundus examination was done with both + 90D and indirect ophthalmoscope. Fundus photos were taken using Canon CF1 Fundus Camera. Height and weight were measured to calculate the BMI. Blood was collected from the patient under aseptic conditions and CRP was assessed through laboratory analysis (Turbidometry Technique).

Results: Out of total 100 patients, most of the cases 51(51%) were in age group of 46-60 years. Majorities of the cases 54% were females. Most of the cases (59%) had 6-10 years of duration of diabetes. 52% patients were without retinopathy and 48% patients were with diabetic retinopathy. NPDR was seen in (26) most of the patients. NPDR+CSME was seen in 10 patients. 6 patients had NPDR+CSME. PDR was seen in 7 patients. PDR+CSME was seen in 5 cases of diabetic retinopathy. 3 cases had duration 6-10 years of diabetic retinopathy. Majorities of cases had duration 6-10 years of DM. Diabetic retinopathy had significantly higher BMI as compared to normal diabetic patients (p=0.028). The mean CRP levels in various types of DR were 2.67 mg/L in NPDR, 2.98 mg/L in NPDR with CSME, 3.8 mg/L in PDR, and 4.0 mg/L in PDR with CSME. Significantly high values of mean CRP were observed in patients with severe forms of PDR and PDR with CSME.

Conclusions: CRP level is significantly increased in diabetic retinopathy patients as compared to without diabetic retinopathy. Higher level of inflammatory activity seen in retina due to higher level of CRP in patients of diabetic retinopathy with PDR and CSME.

Keywords: Diabetic retinopathy, CRP level, Duration of Diabetes mellitus, BMI.

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Introduction

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% [3].

Approximately 93 million individuals worldwide are affected by DR. The prevalence of DR is about 77.3% in patients with type 1 diabetes and 25.1% in those with type 2 diabetes mellitus (T2DM) [4].

Since it is a neurodegenerative microvascular complication, its prevalence increases with the duration of disease and creates an increased threat to vision and causes blindness [5]. Growing evidences suggests that increased oxidative stress and inflammation leads to the impairment of neurovascular structures which is the key element in the development of DR [6, 7].

Pathogenesis and progression of DR can be divided in to two stages: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). Microaneurysms, hemorrhages, cotton-wool patches, soft and hard exudates are seen in NPDR, while neovascularization of the retina

(NVE), disc (NVD), iris (NVI) or angle (NVA), pre-retinal vitreous hemorrhages and resultant tractional retinal detachment comprises of PDR [8,9]. The pathophysiology of DR includes altered metabolic pathways, oxidative stress, and inflammation. Inflammatory mediators such as C-reactive protein (CRP), Tumor Necrosis Factor-a (TNF-a), and interleukin-6 (IL-6) play an important role in the pathophysiology of diabetic retinopathy, according to available literature. Some of the inflammatory mediators involved in both systemic and local inflammation have been investigated as potential biomarkers of DR [10].

One of these markers is C-reactive protein (CRP). C-reactive protein (CRP) was discovered in 1930. The liver produces pentraxin-family calcium-dependent ligand binding protein CRP in response to IL-6. It is an acute phase protein that serves as a marker for inflammation and tissue damage. CRP has been linked with macrovascular disease [11]. Some studies have revealed a correlation between CRP levels and the occurrence of DR in both type 1andtype 2 diabetic individuals [12]. Objectives of the present study was to Correlate the C-Reactive Protein levels with severity of Diabetic Retinopathy.

Material & Methods

The present study was conducted at the Department of Ophthalmology, Shree Krishna Medical College & Hospital, Muzaffarpur, Bihar, India during a period from July 2025 to December 2025.

A total of 100 diabetic patients who attended OPD of ophthalmology were randomly selected for the study.

The participants were divided into two groups (group A & group B). Group A had 52 patients consisted of diabetic without retinopathy and Group B had 48 patients of diabetes with retinopathy. Out of 100 patients, group had diabetic patients with normal fundus whereas group B had patients were diabetic patients with various stages of diabetic retinopathy. Height and weight measurements were taken and BMI was calculated.

Inclusion criteria included patients with Type II DM, the patients with diabetic retinopathy change and who were willing to participate in the study.

Exclusion criteria included Type I DM, gestational DM, hypertension, cardiac or renal complications, and who were not willing to participate the study.

Methods

Detailed history of the patient was taken that included demographic details, ocular symptoms duration of DM, treatment taken for diabetes, and other associated conditions. A complete assessment was performed to all patients.

Ophthalmic examination included visual acuity, best corrected visual acuity, slit lamp examination for anterior segment were performed. Dilated fundus examination was done with both + 90D and indirect ophthalmoscope. The patients were then classified into different categories patients with no diabetic retinopathy and patients with diabetic retinopathy. Diabetic retinopathy patients were classified as (a) Patients with Non-proliferative Diabetic Retinopathy (b). Patients with Proliferative Diabetic Retinopathy (c). Patients with clinically significant macular edema.

sFundus photos were taken using Canon CF1 Fundus Camera. Height and weight were measured to calculate the BMI. Blood was collected from the patient under aseptic conditions and CRP was assessed through laboratory analysis (Turbidometry Technique).

Statistical Anaysis: Data was analysed by the IBM SPSS software. Mean and standard deviations were observed. Chi square test, student t-test and independent sample Kruskal–Wallis test were applied. P-value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Results

Out of total 100 patients, most of the cases 51(51%) were in age group of 46-60 years.44% patients were in age group of >60 years. Only 5% cases were in age group of 30-45 years. Majorities of the cases 54% were females.

Table 1: Age wise distributions of study participants.

Age group (Years)	No. of patients	Percentages
30-45	5	5%
46-60	51	51%
>60	44	44%
Total	100	100%

Table 2: Gender wise distributions of study participants.

Gender	No. of patients	Percentages
Male	46	46%
Female	54	54%
Total	100	100%

In the present study, out of 100 cases, most of the cases (59%) had 6-10 years of duration of diabetes. Out of 48 diabetic retinopathy cases. Majorities of the cases had also 6-10 years of duration of diabetes.

Table 3: Distribution of patients based on duration of diabetes and diagnosis.

Duration of diabetes (years)	Diagnosis		Total	P-Value
	Normal	Diabetic Retinopathy		
≤5	12(23.08%)	13(27.08%)	25(25%)	0.638
6-10	30(57.69%)	29(60.42%)	59(59%)	
>10	10(19.23%)	6(12.5%)	16(16%)	
Total	52(52%)	48(48%)	100(100%)	

In the present study, out of 48 cases of diabetic retinopathy, NPDR was seen in (26) most of the patients. Among 26 patients of NPDR, 15 patients had 6-10 years of duration of diabetic retinopathy. NPDR+CSME was seen in 10 patients. 6 patients had NPDR+CSME. PDR was seen in 7 patients. Majorities of PDR cases had duration 6-10 years. PDR+CSME was seen in 5 cases of diabetic retinopathy. 3 cases had duration 6-10 years of diabetic retinopathy. Mean BMI between normal diabetic patients and diabetic retinopathy patients was significantly differenced (p=0.028). diabetic retinopathy had higher mean of BMI as compared to normal diabetic patients.

Table 4: Comparison of BMI.

Duration of diabetes (years)	Diagnosis					Total	P-Value
	Normal	NPDR	NPDR+CSME	PDR	PDR+CSME		
≤5	12(23.08%)	6(23.08%)	2(20%)	1(14.28%)	0	21(21%)	0.959
6-10	30(57.69%)	15(57.69%)	6(60%)	4(57.14%)	3(60%)	58(58%)	
>10	10(19.23%)	5(19.23%)	2(20%)	2(28.57%)	2(40%)	21(21%)	
Total	52(52%)	26(26%)	10(10%)	7(7%)	5(5%)	100(100%)	

Table 5: Distribution of patients based on duration of diabetes and diagnosis.

BMI (Kg/m2)	Normal (N-52)	Diabetic Retinopathy (N-48)	P-value
	21.78±2.8	22.96± 2.46	0.028

In the present study, significantly higher mean CRP values were observed in the patients with diabetic retinopathy as compared to those without diabetic retinopathy (P<0.001). The mean CRP levels in various types of DR were 2.67 mg/L in NPDR, 2.98 mg/L in NPDR with CSME, 3.8 mg/L in PDR, and 4.0 mg/L in PDR with CSME. Significantly high values of mean CRP were observed in patients with severe forms of PDR and PDR with CSME.

Table 6: Comparison of mean CRP among normal and different types of diabetic retinopathy (n=100).

CRP	Normal	NPDR	NPDR+CSME	PDR	PDR+CSME	p-value
	2.14±0.4	2.67±1.3	2.98±0.5	3.8±0.7	4.0±0.4	<0.001

Discussions

Diabetic retinopathy (DR) is one of the leading causes of vision impairment worldwide and the primary cause of visual loss among diabetic individuals aged 25 years and older [13]. Vision loss resulting from DR may be secondary to macular edema (ME), hemorrhage from neovascularization, retinal detachment, or neovascular glaucoma. The vast majority of patients with DR remain asymptomatic until the disease has significantly progressed [14]. Given the potential for rapid progression and the effectiveness of early intervention in slowing or reversing vision loss, regular screening for retinal complications in diabetic patients is crucial.

DR is categorized into two major forms: non proliferative and proliferative, based on the presence or absence of abnormal neovascularization originating from the retina. Non-proliferative DR (NPDR) is characterized by microaneurysms, retinal hemorrhages, hard exudates, cotton wool spots, and intraretinal microvascular abnormalities. Visual impairment in NPDR primarily results from ME. NPDR is further classified into mild, moderate, severe, and very severe stages based on the risk of progression to proliferative DR (PDR) [15].

In the present study, the results revealed significantly higher levels of CRP among the patients with diabetic retinopathy and among those with CSME. Our analysis revealed no statistically

significant association between duration of diabetes and presence of retinopathy, probably because of limited sample size (P=0.959).

A systematic review and meta-analysis by Song et al. on a series of 3679 patients from 22 studies revealed a potential relationship between CRP level and DR and showed higher blood CRP levels in patients with DR than those without DR [8]. The present study demonstrated that hs-CRP levels in patients with PDR was higher compared with patients with NPDR and PPDR, which is consistent with the findings of Chen et al, and Jia et al, suggesting a positive association of hs-CRP with the severity of DR [16,17]. Several studies have referred to hs-CRP instead of CRP. In fact, hs-CRP is CRP that is detected using immunoassay methods to increase the sensitivity for CRP quantification in acute phase responses [11].

Blum et al. [21] conducted a study in a series of 73 patients with diabetes, of which 25 patients showed NPDR stage and 23 patients showed PDR stage. The hs-CRP levels were higher in patients with diabetes than the control group. However, they concluded that patients with diabetes but without retinopathy and those with NPDR had high levels of inflammatory and angiogenic markers, which decreased in patients with PDR. Studies in patients with DR have examined several clinical parameters in NPDR and PDR stage of retinopathy; however, none of the studies looked at the PPDR stage that was investigated in the present study.

In the present study, significantly higher mean CRP values were observed in the patients with diabetic retinopathy as compared to those without diabetic retinopathy (P<0.001). The mean CRP levels in various types of DR were 2.67 mg/L in NPDR, 2.98 mg/L in NPDR with CSME, 3.8 mg/L in PDR, and 4.0 mg/L in PDR with CSME. Significantly high values of mean CRP were observed in patients with severe forms of PDR and PDR with CSME. This shows the role of inflammatory activity in diabetic retinopathy. There was significant differenced seen in BMI of diabetic patients with and without diabetic retinopathy (P=0.028).

These observations are also comparable to that of the present study findings. Nimesh et al. [18] in their study observed that mean CRP levels in patients with PDR were maximum (3.85±2.14 mg/l) followed by very severe NPDR (3.27±1.41 mg/l), severe NPDR (2.80±1.38 mg/l), moderate NPDR (2.77±1.06 mg/l), and mild NPDR (2.73±1.46 mg/l). Sen et al. [19] studied the relationship between CRP, BMI, and diabetic retinopathy in Indian population among 60 patients. The study reported significant difference in CRP between patients with diabetic retinopathy and without diabetic retinopathy (p = 0.000).

This result is similar to that of Kaur et al. [20] with study conducted on 60 diabetic retinopathy patients and divided into 20 cases without diabetic retinopathy, 20 cases of NPDR and 20 cases of PDR. CRP levels in the control group were found to be 2.43 ± 2.9 mg / dl, in the group without diabetic retinopathy 2.98 ± 4.2 mg / dl, in the NPDR group found 7.49 ± 8.37 mg / dl, and group PDR 6.67 ± 4.3 mg / dl, which are statistically significant.

Conclusions

The present concluded the CRP level is significantly increased in diabetic retinopathy patients as compared to without diabetic retinopathy. Higher level of inflammatory activity seen in retina due to higher level of CRP in patients of diabetic retinopathy with PDR and CSME.

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