ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Correlation of C-reactive protein and BMI with severity of diabetic retinopathy

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Submission: 15-12-2022 Revision: 04-03-2022 Publication: 01-04-2022

ABSTRACT

Background: Diabetic retinopathy is one of the complications of diabetes mellitus (DM). The pathogenesis has been attributed to be due to inflammation recently. Similarly, obesity has been found to be risk factor for diabetic retinopathy. **Aims and Objectives:** The aim of the study was to evaluate the changes of C-reactive protein (CRP) in Type 2 DM patients with diabetic retinopathy and to evaluate the relationship of body mass index (BMI) with diabetic retinopathy. **Materials and Methods:** This was a hospital-based cross-sectional study of 98 patients with Type 2 DM both newly diagnosed and known case of DM. The patient's fundus findings were recorded, CRP and BMI were measured to study the correlation. **Results:** This study showed that the mean value of CRP in patient without diabetic retinopathy was 2.28 mg/L while it was 3.01 mg/L in patients with diabetic retinopathy. Among the patients with diabetic retinopathy, the mean CRP was 2.76 mg/L in NPDR, 2.93 mg/L in NPDR with CSME, 3.6 mg/L in PDR, and 3.9mg/L in PDR with CSME. The mean BMI was 22.63 Kg/m² in patients without diabetic retinopathy and 22.92 Kg/m² in patients with diabetic retinopathy. **Conclusion:** The study shows that CRP levels correlate with stage of diabetic retinopathy. The higher levels CRP were found in patients with PDR and CSME presumably due to the higher level of inflammatory activity in retina. Further our study found no correlation of BMI with diabetic retinopathy.

Key words: Body mass index; C-reactive protein; Diabetic retinopathy

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i4.41460

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

The prevalence of diabetes mellitus (DM) is expected to increase from the 2010 global estimate of 220 million, to approximately 366 million by the year 2030, according to the World Health Organization (WHO).[1] The WHO has labeled India as "The diabetic capital of the world" as it has the highest number of diabetics in the world.[2]

Diabetic retinopathy is one of the leading causes of avoidable blindness in developing and developed countries. The prevalence of retinopathy is strongly related to the duration of diabetes.[3] After 20 years of diabetes, nearly all patients with Type 1 diabetes and more than 60% of patients with Type 2 diabetes have some degree of retinopathy.[3] Good glycemic control arrests the development and progression of diabetic retinopathy and prevents visual loss. Diabetic retinopathy causes visual impairment either by direct involvement of capillaries of macula or by complications of proliferative diabetic retinopathy.

It has now been recognized that inflammation plays a key role in the pathogenesis of diabetic retinopathy by contributing to the atherothrombotic process. The studies have shown the role of coagulation factors in diabetic retinopathy in both Type 1 and Type 2 DM. In addition, various inflammatory markers have been found to affect the disease process and progression of diabetic retinopathy.

C-reactive protein (CRP) is one such well known inflammatory marker.[4,5] It is an acute phase reactant. Its relative diagnostic and prognostic role has been determined in many musculoskeletal disorders, liver, and kidney disorders.

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It is involved in endothelial dysfunction and atherogenesis.[5-7] It has been associated with macrovascular disease.[8-10] It has also been associated with non-ocular microvascular complications of diabetes.[11,12] However, the role of CRP in diabetic retinopathy has not been conclusively elucidated yet. Elevations in the level of markers of inflammation can be attributed to hyperglycemia, advanced glycation end products, and increased body mass index (BMI).

BMI, the most commonly used index of body mass, is calculated by dividing the weight in kilograms by the square of height in meters.[13] It has been shown that being overweight and obese are two risk factors for DM.[14] Thus, overweight and obese people can be more vulnerable to develop DR.[15] However, various studies had varying results regarding the association of DR with BMI. In this study, we attempt to see if CRP can prove to be a marker for detection of diabetic retinopathy as well the association of BMI and diabetic retinopathy.

Aims and objectives

The aim of the study was to evaluate the changes of CRP in Type 2 DM patients with diabetic retinopathy and to evaluate the relationship of BMI with diabetic retinopathy.

MATERIALS AND METHODS

This cross-sectional hospital-based comparative study was done in Department of Ophthalmology, Sri Manakula Vinayagar Medical College and Hospital. It is a multispecialty hospital located 17 km away from the main town of Pondicherry, a union territory in South India.

Approval letter of ethical clearance with code number: 65/2016 was obtained from the Research Committee and Institutional Ethical Committee of Sri Manakula Vinayagar Medical College and Hospital, Puducherry, before initiation of the study.

The study was done for a period of 18 months. Ninety-eight patients who attended OPD of ophthalmology were randomly selected for the study. Sample size was calculated based on a previous study cited reference article using OpenEpi Software version 3.0, considering confidence interval of 95%.[16]

The participants were divided into two equal groups of 49 participants. Group 1 consisted of diabetic without retinopathy and Group 2 diabetes with retinopathy.

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.

Detailed history of the patient was taken that included demographic details, ocular symptoms duration of DM, treatment taken for diabetes, and other associated conditions. Gross systemic examination was done. Ophthalmic examination included visual acuity, best corrected visual acuity, slit lamp examination for anterior segment. Dilated fundus examination was done with both + 90D and indirect ophthalmoscope. The patients were then classified into different categories based on early treatment diabetic retinopathy study[17] patients with no diabetic retinopathy

a. Patients with Non-proliferative Diabetic Retinopathy
b. Patients with Proliferative Diabetic Retinopathy
c. Patients with Clinically Significant Macular Edema.

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). A total of 98 patients were included in the study. Forty-nine patients were diabetic patients with normal fundus whereas 49 patients were diabetic patients with various stages of diabetic retinopathy. Height and weight measurements were taken and BMI was calculated.

Data analysis

Statistical analysis was done using SPSS 22 version software. Student t-test and independent sample Krusak–Wallis test were applied for comparison of means. Chi-square test was applied to calculate the P value. $P<0.001$ was considered as statistically significant. Categorical data were represented in the form of frequencies and proportions. Continuous data were represented as mean and standard deviation. Multi nominal logistic regression analysis was done to adjust for potential confounders.

RESULTS

Mean age of the participants in the study was 59.92±8.16 (SD) years. About 49% of the study population were males and 51% of the study population were females (Table 1).

Mean duration of diabetes was 8.26±3.9 (SD) years. The mean duration of diabetes among the patients with normal fundus was 6.22 years and that of patients with diabetic retinopathy was 10.10 years. Even though the mean duration was higher in patients with diabetic retinopathy, our analysis revealed no statistically significant association between duration of diabetes and presence of retinopathy (P value – 0.559) (Table 2).

No significant association was observed between duration of diabetes and type of retinopathy (P value 0.661) (Table 3). There was also no significance noted between BMI and retinopathy status (Table 4).

Significantly higher mean CRP values were observed among the patients with diabetic retinopathy as compared to those without diabetic retinopathy (P<0.001). Significantly higher values of mean CRP were observed in patients with severe forms of diabetic retinopathy (P<0.001) (Table 5).

Table 1: Age group and sex distribution

	Frequency	Percentage
Age		
30–45	4	4
46–60	48	49
>60	46	47
Sex		
Male	48	49
Female	50	51

DISCUSSION

Diabetic retinopathy is a sight-threatening microvascular complication of DM. The pathogenesis of diabetic retinopathy involves many inflammatory mediators, CRP being one of them. In this study, we try to investigate the role of CRP in diabetic retinopathy.

The results revealed significantly higher levels of CRP among the patients with diabetic retinopathy and among those with CSME. In the present study, our analysis revealed no statistically significant association between duration of diabetes and presence of retinopathy, probably because of limited sample size (P value 0.661).

The mean value of CRP was found to be 2.28 mg/L in patients without diabetic retinopathy and 3.01 mg/L in patients with diabetic retinopathy. Significantly higher mean CRP values were observed among the patients with diabetic retinopathy as compared to those without diabetic retinopathy (P<0.001). The mean CRP levels in various types

Table 2: Distribution of study participants based on duration of diabetes and diagnosis (n=98)

Duration of diabetes (in years)	Diagnosis		Total n (%)	P value*
	Diabetic Retinopathy n (%)	Normal n (%)		
<5	11 (42.3)	15 (57.7)	26 (100.0)	0.559
6–10	28 (50.9)	27 (49.1)	55 (100.0)	
>10	10 (58.8)	7 (41.2)	17 (100.0)	
Total	49 (100.0)	49 (100.0)	98 (100.0)	

*Chi-square test was applied to test statistical difference in proportions

Table 3: Association between duration of diabetes and type of retinopathy (n=98)

Duration of diabetes (in years)	Diagnosis					Total n (%)	P value*
	Normal n (%)	NPDR n (%)	NPDR+CSME n (%)	PDR n (%)	PDR+CSME n (%)		
<5	15 (57.7)	8 (30.8)	2 (7.7)	1 (3.8)	0 (0.0)	26 (100.0)	0.661
6–10	27 (49.1)	15 (27.3)	7 (12.7)	3 (5.5)	3 (5.5)	55 (100.0)	
>10	7 (41.2)	4 (23.5)	2 (11.8)	3 (17.6)	1 (5.9)	17 (100.0)	
Total	49 (50.0)	27 (27.6)	11 (11.2)	7 (7.1)	4 (4.1)	98 (100.0)	

*Chi-square test was applied to test statistical difference in proportion

Table 4: Distribution of study groups based on BMI of the study participants and diagnosis (n=98)

BMI (in Kg/m^2)	Normal (n=49)		Diabetic Retinopathy (n=49)		Difference in mean (95% CI)	P value*
	Mean	SD	Mean	SD		
	22.63	2.7	22.92	2.1	0.29(-0.69-1.3)	0.560

*Student t-test was applied for comparison of means. BMI: Body mass index

Table 5: Comparison of mean CRP among different types of diabetic retinopathy (n=98)

CRP	Normal	NPDR	NPDR+CSME	PDR	PDR+CSME	P value*
	2.28±0.5	2.76±1.1	2.93±0.4	3.6±0.4	3.9±0.3	<0.001

*Independent sample Kruskal–Wallis test was applied for comparison of means. CRP: C-reactive protein

of DR were as follows: 2.76 mg/L in NPDR, 2.93 mg/L in NPDR with CSME, 3.6 mg/L in PDR, and 3.9 mg/L in PDR with CSME. Significantly high values of mean CRP were observed in patients with severe forms of PDR and CSME. This shows the role of inflammatory activity in diabetic retinopathy. The mean BMI in patients without diabetic retinopathy was 22.63 kg/m^2, while it was 22.92 kg/m^2 in patients with diabetic retinopathy. No significant difference was observed in BMI of diabetic patients with and without diabetic retinopathy (P value 0.560).

When we analyzed literature, the relationship between acute phase markers of inflammation and diabetic retinopathy was studied by Kaur et al.,[18] It showed that CRP value was high in patients with retinopathy as compared to normal controls and diabetics without retinopathy (P<0.05). These observations are comparable to that of the present study findings. Nimesh et al.,[19] 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.,[20] 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). whereas no such significant difference was observed in BMI between two groups (P=0.12). Study by Zhou et al.,[21] also showed same results.

CONCLUSION

The present study shows that CRP levels correlate with the stage of diabetic retinopathy. The higher levels of CRP were found in patients with PDR and CSME, presumably as they have higher level of inflammatory activity in the retina. Furthermore, our study found no correlation of BMI with diabetic retinopathy. Further studies with higher sample size are needed to substantiate the results found in our study.

Limitations of the study

A larger sample size is required in consolidating the findings that we have got in this study. Equal representation of various groups of diabetes such as NPDR, PDR, and CSME would have provided a better picture of the correlation. The use of hsCRP would have proven a more accurate analysis. hsCRP can detect trace elevation of CRP while normal CRP does not tend to do so.

ACKNOWLEDGMENT

NIL

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Authors Contribution:
NNG- Principle investigator, concept, and design of study; **RDK-** Concept, coordination, preparation of manuscript, and revision of manuscript; **NP-** Intellectual concept and statistical analysis; and **SM-** Definition and intellectual content

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Source of Support: Nil, **Conflict of Interest:** None declared.