



TO SEE THE CORRELATION OF C-REACTIVE PROTEIN IN CASES OF DIABETIC MACULAR EDEMA

Ophthalmology

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KEYWORDS

INTRODUCTION

India is called as the “diabetic capital of the world,” with numerous of patients with diabetes expected to be 60.9 million by 2025.

There are approximately 35 million people in India with diabetes, the largest number in any country around the world and this is predicted to rise to 80 million by 2030. Diabetes is known to cause microangiopathy and affects small calibre vessels leading to end organ damage like Diabetic Retinopathy (DR). Diabetic macular edema (DME) affects 20% of patients of diabetic duration >10 years.

In order to prevent blindness from diabetic retinopathy, prevention and early detection are mandatory.

Patients with untreated diabetes are 25 times more likely to become blind due to DR and macular edema as compared to those without diabetes. 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.

C-reactive protein (CRP) is a sign of inflammation in the walls of arteries. Its relative diagnostic and prognostic role have determined in many musculoskeletal disorders, liver, and kidney disorders. But few attempts have been made to show its role in diabetic patients especially in those with retinopathic changes. In this study an attempt was thus made to see if C -reactive protein be a marker for the detection of diabetic retinopathic changes patients. The objective of the study is to see the correlation of CRP in severity assessment of Diabetic Macular Edema. And to see the effect of treatment of DIABETIC MACULAR EDEMA on levels of CRP patients with DME.

METHODS

This study was conducted as an OPD based cross sectional study in upgraded department of ophthalmology, SVBP hospital attached to LLRM Medical College to see the correlation of CRP in severity assessment of Diabetic Macular Edema and to establish if CRP can be used as screening tool for Diabetic retinopathy.

The school-based study was conducted in OPD of Upgraded department of ophthalmology, LLRM Medical College.

The study was carried out from July 2021 to July 2022. To achieve the aims and objectives of the study, sample size was calculated as 96, assuming that there is correlation of CRP level in severity assessment of diabetic macular edema in 50% of patients and absolute precision 10% at 95% confidence interval. The sample size of beneficiaries was calculated as:

$$n = (1.96)^2 \frac{p+q}{d^2}$$

$$= 3.84 \times 50 \times (100-50) / (10)^2 = 96$$

In order to achieve the objectives of the study, cross-sectional study with simple random sampling was done.

The participants were divided into two equal groups. Group 1 consisted of patients with diabetic macular edema and Group 2 consist

of patients with diabetic retinopathy but without diabetic macular edema.

Different measuring tools were used such as Pretested semi-structured questionnaire, Basic ocular examination, Vision acuity, KFT, LFT, Blood sugar, Optical Coherence Tomography, HBA1C, CRP levels, Fundus examination

All data was analyzed using statistical analysis was done using SPSS software. P value <0.001 was considered as significant.

RESULTS

Table No. 1- Types of Retinopathy in association with duration of Diabetes

Duration of diabetes (in yrs)	NPDR N(%)	NPDR +DME N(%)	PDR N(%)	PDR+DME N(%)
<5yrs	01(25%)	0(0%)	0(0%)	0(0%)
5-10yrs	0(0%)	4(67%)	12(27%)	3(7%)
11-15yrs	02(50%)	1(16.5%)	13(29.5%)	18(43%)
>15 yrs	01(25%)	1(16.5%)	19(43.5%)	21(50%)
Total	04(100%)	06(100%)	44(100%)	42(100%)

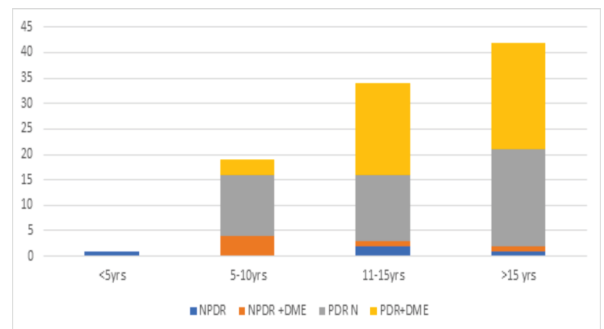
NPDR- Non Proliferative Diabetic Retinopathy

PDR- Proliferative Diabetic Retinopathy

DME- Diabetic Macular Edema

Among study participants those who were having NPDR, 50% of them were having diabetes for 11 to 15 years, 25% of them for having diabetes for more than 15 years and 25% of them were having for less than five years. Among study participants who were having NPDR + DME, 67% of them were having diabetes for 5 to 10 years, 16.5% of them were having diabetes for 11 to 15 years and 16.5% of them were having diabetes for more than 15 years.

Among study participants, those who were having PDR, 43.5% of them were having diabetes for more than 15 years, 29.5% of them were having diabetes for 11 to 15 years and 27% of them were having diabetes for 5 to 10 years. Among study participants, those who were having PDR + DME, 50% of them were having diabetes for more than 15 years, 43% of them were having diabetes for 11 to 15 years and 7% of them were having diabetes for 5 to 10 years.



Types of Retinopathy in association with duration of Diabetes

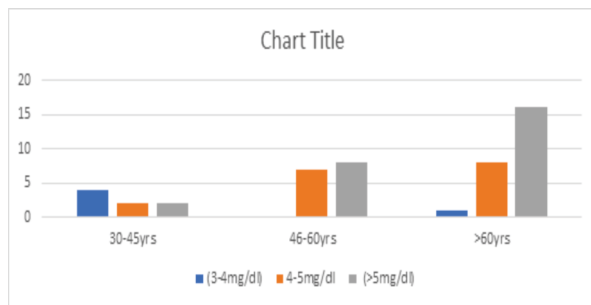
Table No.2- CRP levels in association with age among participants having Diabetic Retinopathy with Diabetic Macular Edema (N=48)

Age	CRP level(3-4mg/dl)	CRP level(4-5mg/dl)	CRP level (>5mg/dl)	P value
30-45yrs	4(80%)	2(12%)	2 (8%)	<0.05
46-60yrs	0(0%)	7(41%)	8(31%)	
>60yrs	1(20%)	8(47%)	16(61%)	
Total	5(100%)	17(100%)	26(100%)	

Among those participants who were having diabetic retinopathy with diabetic macular edema and CRP level between 3 to 4mg/dl, 80% of them were among 30 to 45 years and 20% were above 60%.

Among those study participants who were having CRP level in the range of 4 to 5mg/dl, 47% of them were above 60 years, 45% of them were among 46 to 60 years and 12% of them were among 30-45 years.

Among those study participants who were having diabetic retinopathy with diabetic macular edema and CRP level more than 5mg/dl, 61% of them were above 60 years, 31% of them were in between 46 to 60 years and 8% of them were among 30 to 45 years.



CRP levels in association with age among participants having Diabetic Retinopathy with Diabetic Macular Edema

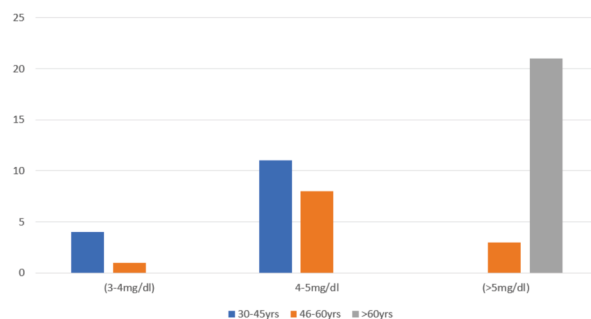
Table No.3- CRP levels in association with age among participants having Diabetic Retinopathy without Diabetic Macular Edema (N=48)

Age	CRP level(3-4mg/dl)	CRP level(4-5mg/dl)	CRP level (>5mg/dl)	P value
30-45yrs	4(80%)	11(58%)	0(0%)	<0.05
46-60yrs	1(20%)	8(42%)	3(12.5%)	
>60yrs	0(0%)	0(0%)	21(87.5%)	
Total	5(100%)	19(100%)	24(100%)	

Among those participants who were having diabetic retinopathy without diabetic macular edema and CRP level between 3 to 4mg/dl, 80% of them were among 30 to 45 years and 20% were in between 45 to 60 years.

Among those study participants who were having CRP level in the range of 4 to 5mg/dl, 58% of them were among 30-45 years and 42% of them were among 46 to 60 years.

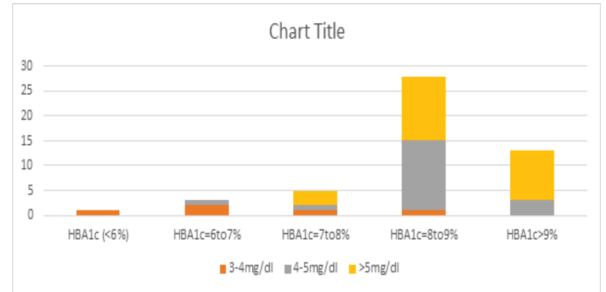
Among those study participants who were having diabetic retinopathy with diabetic macular edema and CRP level more than 5mg/dl, 87.5% of them were above 60 years and 12.5% of them were in between 46 to 60 years.



CRP levels in association with age among participants having Diabetic Retinopathy without Diabetic Macular Edema

Table No. 4- CRP levels in association HBA1c level in Participants having Diabetic Retinopathy without Diabetic Macular Edema. (N-48)

CRP levels	HBA1c (<6%)	HBA1c (6-7%)	HBA1c (7-8%)	HBA1c (8-9%)	HBA1c (>9%)	P value
3-4mg/dl	1(100%)	2(66%)	1(20%)	1(3.5%)	0(0%)	>0.05
4-5mg/dl	0(0%)	1(34%)	1(20%)	14(50%)	3(23%)	>0.05
>5mg/dl	0(0%)	0(0%)	3(60%)	13(46.5%)	10(77%)	>0.05
Total	1(100%)	3(100%)	5(100%)	28(100%)	13(100%)	



Among study participants having diabetic retinopathy without diabetic macular edema and HBA1C 6-7% percent, 100% were having CRP level in the range of 3 to 4mg/dl.

Among study participants having diabetic macular edema with HBA1C 7-8%, 34% were having CRP level in range of 4 to 5mg/dl , 66% were having CRP level in the range of 3 to 4mg/dl.

Among the participants with HBA1C 8-9%, 46.5% of them were having CRP level more than 5mg/dl and 50% were having CRP level in the range of 4 to 5mg/dl.

Among study participants having diabetic retinopathy with diabetic macular edema and HBA1C >9% percent, 77% were having CRP levels more than 5mg/dl and 23% of them when having CRP level in the range of 4 to 5mg/dl.

DISCUSSION

DM is reaching epidemic proportions in the world today. Inflammation is thought to play an inevitable role in DR. In this study, the role of CRP as an inflammatory biomarker on severity of DME along with HbA1c was analyzed, also this study analyzed to see the effect of treatment of DIABETIC MACULAR EDEMA on levels of CRP. The study also showed that patients with positive CRP were found to have elevated HbA1c values. 96 patients participated in the present study. The present study concluded that CRP is a useful marker to assess the severity of DME.

HbA1c is an established marker for assessing glycaemic control and also proved to be significantly associated with the severity of DR. Patients with poor glycaemic control need to be counselled about earlier development of DR and accelerated progression of severity of DR. Our study signifies the critical role of inflammation and metabolic control in the pathogenesis of DR and DME as indicated by CRP and HbA1c.

Patients with macular edema were treated with intravitreal injections and were followed-up. Results showed no significant change in CRP levels after treatment denoting that it is not the important biomarker for follow up of patients after treatment.

CONCLUSION

The study revealed the following findings:

- 1) Maximum participants having diabetic retinopathy with or without diabetic macular edema, were having diabetes for more than 15 years. Thus, duration of diabetes was not found to be associated with diabetic macular edema.
- 2) Maximum participants, who were having diabetes for more than 15 years were having PDR+DME followed by PDR and least were having NPDR. Among participants those who were having diabetes for less than 5 years, no one was having PDR+DME. Results were found to be statistically significant. Thus, it was found that duration of diabetes was associated with type of diabetic retinopathy.
- 3) It was found that among patient having diabetic retinopathy with

- or without diabetic macular edema who were more than 60 years, mostly had CRP level $>5\text{mg/dl}$. But there was no association found between age and CRP levels among patient with diabetic retinopathy.
- 4) Majority of participants who were having HBA1C more than 9% were also having higher CRP levels than those who have HBA1C $<6\%$. Thus there was association between HBA1C and CRP levels.

REFERENCES:

1. Raman R, Verma A, Pal SS, Gupta A, Vaitheeswaran K, Sharma T. Influence of glycosylated hemoglobin on sight-threatening diabetic retinopathy: A population-based study. *Diabetes Res Clin Pract* 2011;92:168-73.
2. Raman R, Rani PK, Kulothungan V, Racheppalle SR, Kumaramanickavel G, Sharma T. Influence of serum lipids on clinically significant versus nonclinically significant macular edema: SN-DREAMS report number 13. *Ophthalmology* 2010;117:766-72.
3. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: the Chennai Urban Rural Epidemiology Study (CURES) eye study. *Invest Ophthalmol Vis Sci*. 2005 Jul;46(7):2328-33
4. Morimoto Y, Conroy SM, Ollberding NJ, Kim Y, Lim U, Cooney RV, Franke AA, Wilkens LR, Hernandez BY, Goodman MT, Henderson BE, Kolonel LN, Le Marchand L, Maskarinec G. Ethnic differences in serum adipokine and C-reactive protein levels: the multiethnic cohort. *Int J Obes (Lond)*. 2014 Nov;38(11):1416-22. doi: 10.1038/ijo.2014.25. Epub 2014 Feb 13.
5. Schmidt AM, Hori O, Chen JX, Li JF, Crandall J, Zhang J, Cao R, Yan SD, Brett J, Stern D. Advanced glycation endproducts interacting with their endothelial receptor induce expression of vascular cell adhesion molecule-1 (VCAM-1) in cultured human endothelial cells and in mice. A potential mechanism for the accelerated vasculopathy of diabetes. *J Clin Invest*. 1995 Sep;96(3):1395-403