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Research Article

CORRELATION OF C-REACTIVE PROTEIN WITH SEVERITY OF DIABETIC RETINOPATHY

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ABSTRACT

Objectives: To study the correlation of C-reactive protein (CRP) with severity of diabetic retinopathy (DR) in patients with type II diabetes.
Methods: This prospective, cross sectional study consisted of hundred patients with DR (classified by using Early Treatment Diabetic Retinopathy Study, ETDRS) who were examined as in keeping with the predesigned proforma. Precise ophthalmological examination was done; fasting and post-prandial blood sugar (FBS and PPBS), Glycosylated hemoglobinHbA1C, CRP and serum lipid profile, serum creatinine and uric acid had been assessed.
Results: The present study showed that CRP ranges have statistically significant correlation with DR and also full-size association between increasing lipid levels and DR ($p<0.05$) was seen. Serum LDL stages and triglycerides additionally confirmed statistically good sized correlation with growing severity of DR.
Conclusion: CRP may be relied as a watchdog biomarker for progression of DR, also persistently deranged lipid profile may be targeted for purpose of remedy, in known diabetics for prevention of advanced DR.

INTRODUCTION

Diabetic retinopathy (DR) is the major cause of blindness both in developed and developing countries. In 2010, of an estimated 285 million diabetics, one-third have some form of DR and out of these, one-third have vision threatening DR(Bourne *et al*., 2013). According to a recent study, there are about 93 million people with DR and 17 million with PDR worldwide (Yau *et al*., 2012).

So early detection by identifying the risk factors for DR and timely intervention is mandatory. Duration of diabetes is the strongest predictor for DR(Wong *et al*., 2009). Few studies have shown a positive relationship of serum cholesterol and low-density lipoprotein levels with retinal hard exudates. An understanding of relationship between various grades of diabetic retinopathy with lipid profile will be helpful in stratification and tailoring of anti-diabetic and lipid lowering treatment for diabetic retinopathy to retard its progression (Bardosono & Arus Victor, 2008).

C-reactive protein (CRP) is acute phase reactant, which is a sensitive and non-specific marker of inflammation and tissue damage. The association between CRP and systemic diseases has been studied broadly and a large amount of published data showed that higher CRP levels correlate significantly with increased risk of atherosclerosis, cardiovascular diseases and diabetes mellitus (Lim *et al*., 2010).

The relationship between CRP and diabetic retinopathy has been investigated in some studies but there is paucity of data and results are inconsistent.

So the present study was undertaken to study the correlation of CRP levels with severity of diabetic retinopathy in T2DM.

MATERIALS AND METHODS

This was a one-year prospective study, which enrolled 100 patients, who were diagnosed to have Type 2 DM and have some form of DR and attended the outpatient clinic of Department of Ophthalmology and Department of Medicine of J.A. Group of Hospitals, Gwalior (M.P.) from 1st September 2014 to 31st August 2015. Patients included in this study had been diagnosed to have DM as per criteria of American Diabetes Association (2014)(Cameron, 2006).

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After taking informed consent, a detailed history was elicited from all patients and was recorded as per predesigned proforma. Basic information (age, sex, income and educational level), information on lifestyle (such as smoking and alcohol intake), medical history (such as medication, the use of insulin and history of systemic diseases) and family history of diseases were elicited from the interview. The duration of diabetes was defined as the interval between the first diagnosis and the time of enrollment into the present study. Patients with severe media opacity preventing the classification of retinopathy, with shallow anterior chamber or angle-closure glaucoma preventing mydriasis were excluded. The Ethical Committee approved the study protocol. A general physical examination was followed by a comprehensive ophthalmological examination including corrected visual acuity and a thorough anterior segment examination. Intraocular pressure was recorded using Goldman Applanation Tonometry. A detailed fundus examination was done by indirect ophthalmoscopy along with slit lamp biomicroscopy and seven fields 30° color fundus photographs were taken through dilated pupils for all patients using a digital fundus camera.

Overnight fasting blood samples were collected for measurement of fasting blood sugar, FBG, glycosylated hemoglobin (HbA1c), serum creatinine and uric acid, lipid profile [levels of total cholesterol, triglycerides, high-density (HDL) and low-density lipoprotein (LDL) cholesterol. CRP concentration was measured through particle-enhanced immunonephelometry, using an automated analyzer. Data was analyzed by Chi Square Test and Analysis Of Variance (ANOVA).

RESULTS

Out of 100 DM patients 55 were male and of which 51 had Non Proliferative diabetic retinopathy (NPDR)**,** and 4 had Proliferative diabetic retinopathy(PDR). Among 45 females 41 had NPDR and rest had PDR.

Duration of DM and Severity of Diabetic Retinopathy

Grade Of Retinopathy	No. Of Patients	Duration (YRS) MEAN ± SD
MILD NPDR	44	4.5±1.56
MODERATE NPDR	30	9.4±1.61
SEVERE NPDR	11	16.36±2.06
VERY SEVERE NPDR	07	24.14±1.86
PDR	08	28.75±1.98

(NPDR Non Proliferative diabetic retinopathy, PDR Proliferative diabetic retinopathy)

Among the cases, those with PDR and very severe NPDR had the longest duration of diabetes, the mean duration being 28.75±1.98 years and 24.14±1.86 years respectively, followed by those with severe NPDR(16.36±2.06 years), moderate NPDR(9.4±1.61 years), and mild NPDR(4.5±1.56 years).

Lipid Profile & Severity of Diabetic Retinopathy

Grading of Diabetic Retinopathy	Patients (n=100)	Total Cholesterol (mg/dl) Mean ± SD	Triglycerides (mg/dl) Mean ± SD	S.HDL (mg/dl) Mean ± SD	S.LDL (mg/dl) Mean ± SD
Mild NPDR	44	247.2±17.84	155.43±10.28	114.56±2.92	131.52±7.06
Moderate NPDR	30	280±9.23	178.53±5.13	95.4±2.15	151.76±4.96
Severe NPDR	11	310.63±6.72	194±3.68	80.54±6.62	171.45±4.82
Very severe NPDR	07	330.57±7.48	207.71±11.68	66±1.73	181.71±6.29
PDR	08	352.87±6.62	228.75±7.81	43.12±4.22	216.62±6.04

CRP Levels and Severity of Diabetic Retinopathy

Grading of Dr	No. of Patients	CRP Levels (mg/l) MEAN ± SD
Mild NPDR	44	2.73±1.46
Moderate NPDR	30	2.80±1.38
Severe NPDR	11	2.77±1.06
Very severe NPDR	07	3.27±1.41
PDR	08	3.85±2.14

Mean CRP levels in patients with PDR was maximum (3.85±2.14mg/l) followed by very severe NPDR (3.27±1.41mg/l), severe NPDR (2.80±1.38mg/l), moderate NPDR (2.77±1.06mg/l) and mild NPDR (2.73±1.46mg/l).

DISCUSSION

The results showed that the CRP level is positively correlated with progression of DR. Comparing the different DR severities showed that the CRP level in the PDR group was also higher than that in the NPDR group. These result indicated that CRP level may be related to the severity of DR.

DR is a micro-vascular complication of DM, which is mainly due to the long-term high blood glucose (Gao *et al*., 2001). Many studies have investigated the relationship between CRP level and DR, but the conclusions were not consistent. The inconsistent conclusions may be due to various reasons such as including other clinical parameters other than CRP (duration of DM and BMI), the varying definitions of DR, the study design method.

Schram *et al*. researching the micro-vascular complications and cardiovascular disease in type 1 diabetes found that there were statistically significant differences among the three groups (diabetes without retinopathy, NPDR, and PDR) in terms of CRP concentration, but the differences disappeared after BMI values were adjusted (Schram, Chaturvedi, Schalkwijk, Fuller, & Stehouwer, 2005). Izuora *et al*. also obtained similar results (Izuora *et al*., 2005). At the beginning of the study, they found that there was a significant relationship between the grades of retinopathy and CRP. However, after controlling for age, duration of diabetes, sex, and BMI, the significance was lost. The duration of diabetes may also affect the study results. A study by Mysliwska *et al*. showed that the increase in CRP concentration was consistent with the prolonged duration of diabetes and the changes seemed to be significant based on the statistics (Ryba-Stanisławowska, Rybarczyk-Kapturska, Myśliwiec, & Myśliwska, 2014). Some studies demonstrated that CRP level in patients with PDR was higher than in NPDR patients (Song *et al*., 2015). The results were consistent with the research by Mysliwska.

In the detection of CRP concentration, some studies have referred to the HsCRP. In fact, HsCRP, which is higher than CRP in only the detection accuracy, can detect lower concentrations of CRP and is not a new biomarker(Waldhoer, Haidinger, Wald, & Heinzl, 2006).

Various studies have proven the role of elevated serum lipids with macro vascular complications of DM like coronary artery disease but studies of association of lipids with specific micro vascular complications of DM like retinopathy have shown varying results. Dornan *et al* (1982) first showed the an association of LDL cholesterol with diabetic retinopathy(Dornan, Carter, Bron, Turner, & Mann, 1982). Our

study also showing similar results and showed positive correlation of higher cholesterol, TG and LDL values with worsening grades of DR. An Indian study by Sachdev *et al* proved that cholesterol and LDL are risk factors for retinal hard exudates in Type II DM in North Indian population (Sachdev & Sahni, 2010). Keech *et al* (2007) showed that lipid lowering agent like finofibrate, decreases the progression of DR (Keech *et al*., 2007).

CONCLUSIONS

The present study observed that there is positive correlation between serum CRP levels and DR. Hence CRP can be used as a reliable screening tool for DR.

Conflict of Interest: None to declare

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