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Association of High Sensitivity C-Reactive Protein (hs-CRP) 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 by Behring Nephalometer analyzer system. Fundus examination was done for retinopathy. Result: Out of 75 type 2 DM patients, 49 patients had retinopathy. 18 patients had mild non progressive retinopathy, 30 patients had moderate NPDR, whereas only 1 patient had severe NPDR. High hs-CRP levels were observed with moderate retinopathy and severe retinopathy. Conclusion: The hs-CRP levels were raised in patient with diabetic retinopathy, also hs-CRP levels had association with severity of diabetic retinopathy.***

Keywords:

1. Introduction

Diabetic retinopathy (DR), major microvascular 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 [1]. DR can be divided into non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). In the natural course, approximately 50% of patients with very severe NPDR progress to PDR within 1 year.

C-reactive protein, an acute-phase reactant produced by liver, is an extremely sensitive marker of systemic inflammation. The recent development of high-sensitivity assays for CRP (hs-CRP) has permitted detection of even mild elevation of CRP, even within the normal range. It is perceived that chronic low-grade inflammation as evidenced by elevated hs-CRP might potentially be a cause of underlying etiology and manifestations of type 2 diabetes. However, the role of CRP in the pathogenesis of DR is still unknown [2].

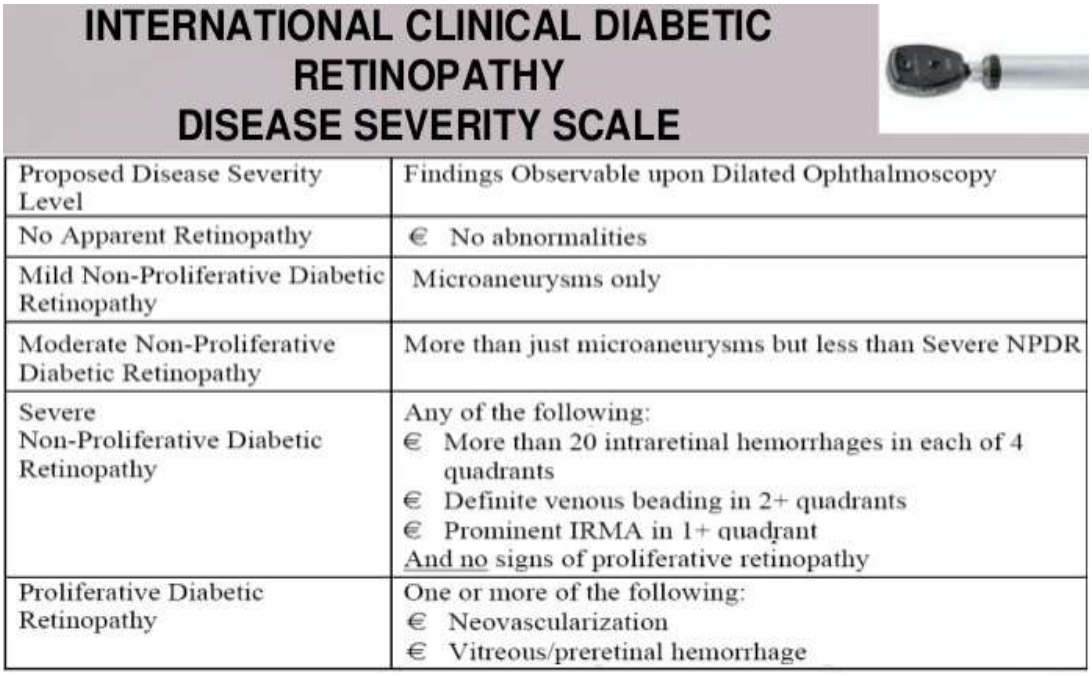
Many clinical studies conducted to investigate the association between CRP level and DR have been inconclusive. Some studies suggest that CRP level is associated with DR and with the severity of the disease [3-5]. However, some studies provide different or even opposite conclusions [6-8]. Therefore, this study was designed to study an association of hs-CRP with diabetic retinopathy in type 2 DM patients. We also saught to ascertain the correlation of hs-CRP levels with severity of diabetic retinopathy.

2. Material and Methods

This observational study was carried out in 75 patients with Type 2 DM (according to WHO criteria), both newly diagnosed and known cases of DM, admitted in Medicine ward and not suffering from any active or chronic inflammatory diseases on interview and were confirmed to be in the normal range for serum conventional CRP (under 4.0 mg/l) and leucocytes count.

Fundus examination of the patients were examined for the retinopathy by ophthalmologist. A five-stage disease severity classification for DR was applied according to the International Classification of Diabetic Retinopathy [9]. DR grade was evaluated for both eyes, and higher grade was recorded for each person.

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INTERNATIONAL CLINICAL DIABETIC RETINOPATHY DISEASE SEVERITY SCALE

Proposed Disease Severity Level	Findings Observable upon Dilated Ophthalmoscopy
No Apparent Retinopathy	€ No abnormalities
Mild Non-Proliferative Diabetic Retinopathy	Microaneurysms only
Moderate Non-Proliferative Diabetic Retinopathy	More than just microaneurysms but less than Severe NPDR
Severe Non-Proliferative Diabetic Retinopathy	Any of the following: € More than 20 intraretinal hemorrhages in each of 4 quadrants € Definite venous beading in 2+ quadrants € Prominent IRMA in 1+ quadrant And no signs of proliferative retinopathy
Proliferative Diabetic Retinopathy	One or more of the following: € Neovascularization € Vitreous/preretinal hemorrhage

The hs-CRP concentration was measured using a Behring Nephalometer analyzer system. Serum hs-CRP level below 1 mg/l indicates low risk, 1-3 mg/l average risk, and 3-10 mg/l very high risk [10]. Glycaemic control was evaluated by measuring glycated haemoglobin (HbA1c) levels. Data of BMI, lipid profiles were also collected for each participant.

3. Results

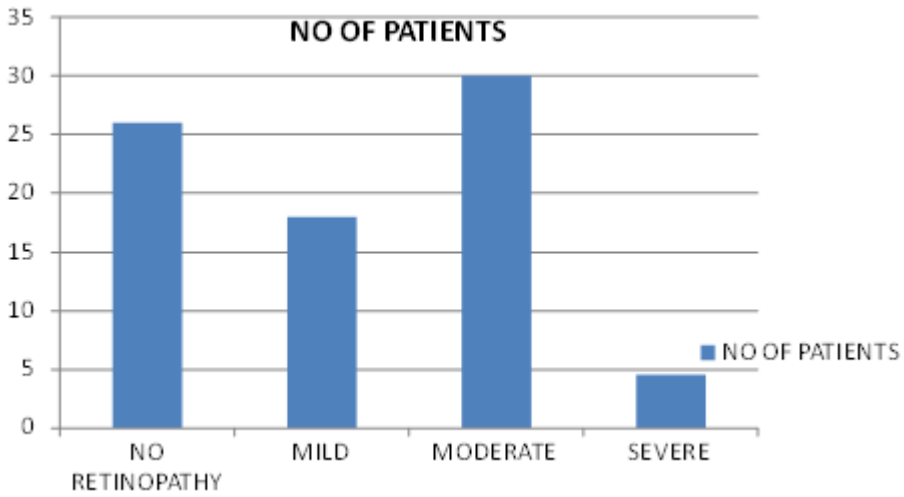
Out of 75 total patients, 49 (65.33%) had retinopathy. 18 (24%) patients had mild non progressive retinopathy, 30 (40%) patients had moderate NPDR, whereas only 1 (1.33%) patient had severe NPDR. High hs-CRP levels were observed with moderate retinopathy and severe retinopathy.

Table 1: Baseline characteristics of cases

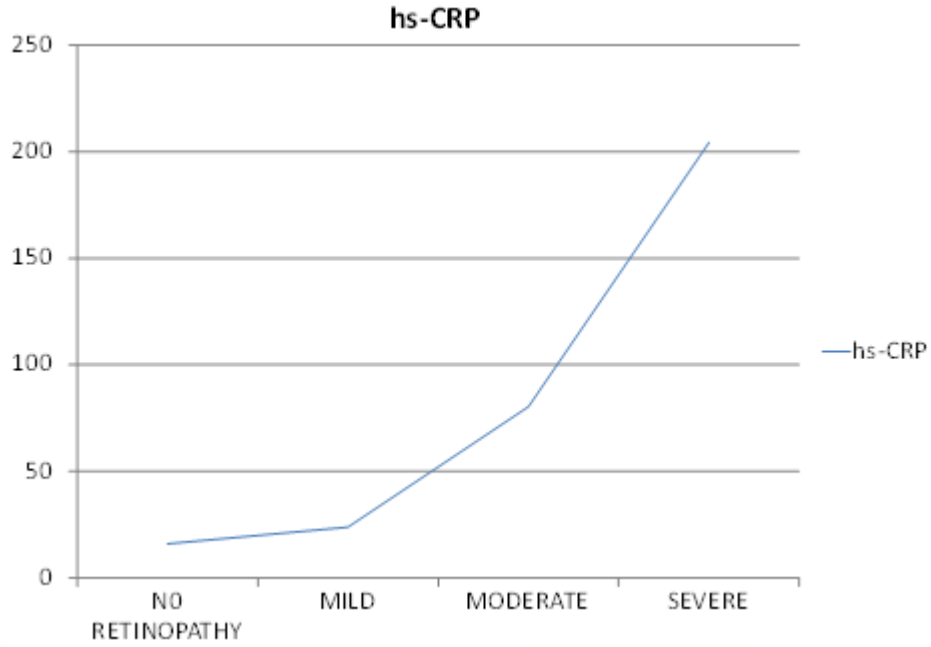
Characteristics	Mean SD
Age (years)	62.4 12.1
Sex Male Female	 47 28
BMI (Kg/m^2)	26.53 3.05
HbA1C (%)	8.63 2.02
BSL (gm/dl) Fasting Post prandial	 202.4616.2 298.1314.6

Table 2: Correlation of hs-CRP levels in retinopathy stages

Level of Retinopathy	No. of cases	hs-CRP levels
No retinopathy	26	15.95 3.1
Mild NPDR	18	23.70 8.6
Moderate NPDR	30	80.23 14.04
Severe NPDR	01	204 19.16



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Fundus of patient with moderate diabetic retinopathy

4. 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.

In the present study, we found indications of an association between elevated levels of hs-CRP and more advanced degrees of diabetic retinopathy. Our findings are compatible with the findings in some, but not all studies. For instance, among 543 patients in a nested case-control study of the EURODIAB study, higher plasma levels of CRP were found in type 1 diabetic patients with nonproliferative diabetic retinopathy and PDR compared to patients without retinopathy [11]. However, the authors did not find an association between the level of CRP and the severity of DR. In the Hoorn study [12], a large population-based cohort study of 625 adults, higher CRP was associated with the prevalence of any DR.

As CRP is a well-known inflammatory marker it would be expected to be elevated in patients with poor glycemic status. In our study, the hs-CRP levels were raised in patient with diabetic retinopathy, also hs-CRP levels showed association with severity of diabetic retinopathy.

References

[1] Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care.2012;35:556–564.

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[2] Lim LS, Tai ES, Mitchell P, Wang JJ, Tay WT, Lamoureux E, et al. C-reactive Protein, Body Mass Index, and Diabetic Retinopathy. Investigative Ophthalmology & Visual Science.2010;51:4458–4463.
[3] Budak YU, Akdogan M, Huysal K. Relationship of PON1 activity and hsCRP concentration with disease status in patients with type 2 diabetes mellitus with and without retinopathy. International Journal of Diabetes in Developing Countries.2013;33:40–45.
[4] Jia ZT, Liu CY, Li H. Changes of the concentration of serum Ischemia modified albumin and high sensitivity c-reactive protein in type 2 diabetic patients with retinopathy. Chinese Journal of Ophthalmology.2009;45:805–808.
[5] Wang XL, Dai Y, Chen XH. Changes of the concentration of serum adiponectin and high sensitivity C-reactive protein in type 2 diabetes mellitus patients with retinopathy. International Journal of Ophthalmology.2010;10:1699–1701.
[6] Blum A, Socea D, Ben-Shushan RS, Keinan-Boker L, Naftali M, Segol G, et al. A decrease in VEGF and inflammatory markers is associated with diabetic proliferative retinopathy. Eur Cytokine Netw.2012;23:158–162.
[7] Gholamhossein Y, Behrouz H, Asghar Z. Diabetic retinopathy risk factors: plasma erythropoietin as a risk factor for proliferative diabetic retinopathy. Korean J Ophthalmol.2014;28:373–378.
[8] Gustavsson C, Agardh E, Bengtsson B, Agardh CD. TNF-(alpha) is an independent serum marker for proliferative retinopathy in type 1 diabetic patients. Journal of Diabetes and its Complications.2008;22:309–316.
[9] Wilkinson CP, Ferris 3rd FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003;110(9):1677–82.
[10] Pfutzner A, Forst T. High-sensitivity C-reactive protein as cardiovascular risk marker in patients with diabetes mellitus. Diabetes Technol Ther 2006; 8:28-36.
[11] Schram MT, Chaturvedi N, Schalkwijk CG, Fuller JH, Stehouwer CD. EURODIAB Prospective Complications Study Group. Markers of inflammation are cross-sectionally associated with microvascular complications and cardiovas- cular disease in type 1 diabetes – the EURODIAB Prospective Complications Study. Diabetologia 2005; 48:370–378.
[12] van Hecke MV, Dekker JM, Nijpels G, Moll AC, Heine RJ, Bouter LM, et al. Inflammation and endothelial dysfunction are associated with retinopathy: the Hoorn Study. Diabetologia. 2005;48(7):1300–6.

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