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Association of Dyslipidemia with Clinically Significant Macular Edema (CSME) in Type – II Diabetes Mellitus

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Abstract **Original Research Article**

Aim: To observe the association between dyslipidemia and CSME in Type – II diabetes mellitus. ***Method:*** With convenience type of sampling technique 36 patients of diabetic retinopathy (DR) with CSME (Group–I) and another 35 patients of DR without CSME (Group – II) aged > 40 years were selected in Bangabandhu Sheikh Mujib Medical University (BSMMU) for this case control study from March'2013 to March'2014. Diagnosis of DR and CSME were carried out by history, clinical examination, fasting blood glucose (FBG), blood glucose 2 hours after breakfast, HbA1c (glycated hemoglobin), color fundus photograph (CFP) and optical coherence tomography (OCT) of macula as per ETDRS (Early treatment diabetic retinopathy study) criteria. Then fasting lipid profile was measured and compared between the groups. ***Result:*** Between two groups age, sex and occupation were matched. Dyslipidemia was present in 32 (88.9%) cases in Group–I and in 18 (51.4%) cases in Group – II, (p =0.001). Mean Total Cholesterol(TC) (211.8 mg/dl), Low Density Lipoprotein(LDL) (141.6 mg/dl) and Triglyceride(TG) (207 mg/dl) in Group – I were significantly higher than mean Total Cholesterol (183.3 mg/dl), Low Density Lipoprotein (118.5 mg/dl) and **Triglyceride** (143.5 mg/dl) in Group –II (p = < 0.05). But High Density Lipoprotein (HDL) was significantly lower in group- I (35.8 mg/dl) than group -II (41.1 mg/dl). ***Conclusion:*** Diabetic retinopathy with CSME has close association with dyslipidemia.

Keywords: Diabetic retinopathy, CSME, dyslipidemia.

INTRODUCTION

Diabetic retinopathy (DR) is an important ocular complication of diabetes mellitus as its management is very difficult. Because most of the time DR progresses and develop complications leading to blindness. To know about the factors related to diabetic retinopathy is also important because the number of diabets patients is rapidly increasing all over the world as well as in Bangladesh. Prevalence of diabetes in Bangladesh was 3,196,000 in 2000 which will be increased to 11,140,000 by 2030 [1]. Among diabetic patients, Type-II diabetes accounts for at least 90% of all cases [2]. Usually onset of type -II DM occurs after late thirties. In diabetic retinopathy there is formation of exudate and can affect any part of retina including macula (macular edema) in the form of macular thickening or hard exudates. Hard exudates are caused by chronic localized retinal edema which is composed of lipoprotein and lipid filled macrophages [3]. So there may be a correlation between diabetic retinopathy and dyslipidemia. In diabetic retinopathy clinically significant macular edema (CSME) is a separate entity to give highest attention because changes are related with central and color vision. In ETDRS (Early Treatment diabetic Retinopathy Study), CSME was defined as any thickening or exudates within 500 micrometer of the centre of the macula or retinal thickening of one disc area or larger, any part of which lies within one disc diameter of centre of macula [4]. In DM derangement occurs in lipid metabolism. Serum lipid profile has four components. These are total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL). The term dyslipidemia implies a disorder of lipoprotein metabolism including lipoprotein overproduction or deficiency [5]. Dyslipidemia may be manifested by elevation of the total cholesterol (TC), the "bad" low

density lipoprotein (LDL) cholesterol and/or triglyceride (TG) concentrations, and a decrease in the "good" high- density lipoprotein (HDL) cholesterol concentration in the blood [6]. It has been postulated that the elevation of blood viscosity and alterations in the fibrinolytic system occurs in hyperlipidemia causing hard exudates formation. There may also be incorporation of triglycerides into the cell membrane leading to changes in membrane fluidity and leakage of plasma constituents into the retina. This results in hemorrhage and edema in the retina [7]. Idiculla J *et al.*, 2012, observed that, elevated serum lipids showed a significant association with retinal hard exudate formation, CSME and loss of vision in type -II diabetics. Lipid lowering agents may help in reducing the occurrence of these retinal findings and loss of vision in diabetic patients [8]. ETDRS data suggested that higher levels of serum lipids (triglycerides, low-density lipoproteins, and very-low-density lipoproteins) were associated with increased risk of developing hard exudates in the macula and a decrease in visual acuity [9]. So the relationship of dyslipidemia between the patients of DR with CSME and DR without CSME deserved further investigation.

MATERIALS AND METHODS

Type of Study

Case control study.

Place of Study

Department of ophthalmology, BSMMU.

METHODOLOGY

Period of Study

March' 2013 to March' 2014.

Sampling Technique

Convenience sampling.

Sample Size

Total 71 cases were selected. 36 in Group – I (DR with CSME) and 35 in Group – II (DR without CSME).

Criteria of Study Population

Inclusion Criteria

Patients aged ≥ 40 years, both sexes, diagnosed as a case of DR, having no or mild media opacities.

Exclusion Criteria

Patients having dense media opacities, having macular edema and/or exudate other than DR, retinal artery or vein occlusion, pan retinal photocoagulation done already and Patients taking lipid lowering agents.

RESULT AND OBSERVATIONS

Table I: Distribution of the study patients by patients profile (n=71)

Age (in years)	Group-I (n=36)		Group-II (n=35)		P value
	n	%	n	%	
40-50	14	38.9	9	25.7	
51-60	13	36.1	15	42.9	
61-70	8	22.2	10	28.6	
>70	1	2.8	1	2.9	
Mean±SD	55.39	±8.7	56.09	±8.3	[a]0.731[ns]
Range (min,max)	40	,73	40	,71	
Sex					
Male	29	80.6	22	62.9	[b]0.097[ns]
Female	7	19.4	13	37.1	

ns= not significant,
[a]P value reached from unpaired t-test,
[b]P value reached from chi square test

Table II: Distribution of the study patients by Dyslipidemia (n=71)

Dyslipidemia	Group-I (n=36)		Group-II (n=35)		OR (95% CI)	P value
	n	%	n	%		
Yes	32	88.9	18	51.4	7.56 (1.96-31.69)	0.001[s]
No	4	11.1	17	48.6		

s= significant

Table II shows dyslipidemia in 32(88.9%) patients in Group - I and 18(51.4%) in Group - II.

Table III: Distribution of the study patients by TC, HDL, LDL and TG (n=71)

	Group-I (n=36)		Group-II (n=35)		P value
	n	%	n	%	
TC (Total cholesterol)					
<200 mg/dl (normal)	14	38.9	26	74.3	
≥200 mg/dl (high)	22	61.1	9	25.7	
Mean±SD	211.8	±54.8	183.3	±44.5	0.019[s]
Range (min,max)	100	,314	79	,290	
HDL (High-density lipoprotein)					
<40 mg/dl (low)	25	69.4	12	34.3	
≥40 mg/dl (normal)	11	30.6	23	65.7	
Mean±SD	35.8	±6.4	41.1	±8.7	0.004[s]
Range (min,max)	23	,49	25	,70	
LDL (Lowdensity lipoprotein)					
<130 mg/dl (normal)	21	58.3	33	94.3	
≥130 mg/dl (high)	15	41.7	2	5.7	
Mean±SD	141.6	±42.6	118.5	±26.7	0.008[s]
Range (min,max)	44	,236	65	,198	
TG (Triglycerides)					
<150 mg/dl (normal)	10	27.8	25	71.4	
≥150 mg/dl (high)	26	72.2	10	28.6	
Mean±SD	207	±108	143.5	±58.1	0.003[s]
Range (min,max)	80	,588	50	,298	

s= significant

Mean TC was found 211.8±54.8 mg/dl in Group - I and 183.3±44.5 mg/dl in Group - II. Mean HDL was found 35.8±6.4 mg/dl in Group - I and 41.1±8.7 mg/dl in Group – II. Mean LDL was found 141.6±42.6 mg/dl in Group - I and 118.5±26.7 mg/dl in Group – II. Mean TG was found 207±108 mg/dl in Group - I and 143.5±58.1 mg/dl in Group - II. All the differences were statistically significant ($p<0.05$) between two groups.

Table IV: Correlation between lipids profile with hard exudate (n=71)

Lipids profile	Group-I		Group-II		P value
	Mean±SD mg/dl		Mean±SD mg/dl		
TC					
Hard exudates	211.83	±54.76	171.43	±42.13	[a]0.009[s]
Not hard exudates	-		191.19	±45.23	
P value			[b]**0.062[ns]**		
HDL					
Hard exudates	35.78	±6.4	41.86	±8.41	[a]0.024[s]
Not hard exudates	-		40.67	±9.02	
P value			[b]**0.570[ns]**		
LDL					
Hard exudates	141.56	±42.56	116.14	±20.12	[a]0.006[s]
Not hard exudates	-		120.14	±30.64	
P value			[b]**0.520[ns]**		
TG					
Hard exudates	206	±108	162.05	±61.15	[a]0.001[s]
Not hard exudates	-		115.64	±40.83	
P value			[b]**0.001[s]**		

s=significant, ns= not significant, [a] P value reached from unpaired t-test.

DISCUSSION

In this study, the patients were matched in relation to age and sex,. The age of the patients were ranged from 40 to 73 years (a mean 55.39 ±8.7) in Group – I, and 40 to 71 years (mean 55.09 ±8.3) in Group – II (p = 0.731). In Group – I, BCVA ranged from +0.2 to +1.4 (Log MAR) with a mean of 0.5±0.3 and in Group – II, BCVA ranged from 0 to +1.3 (Log MAR) with a mean of 0.2±0.3. Difference was

significant (p = 0.001). Idiculla J *et al.,* 2012 found similar finding [10]. This difference of visual acuity was due to CSME. It is now established that progression of DR and CSME positively correlated with duration of diabetes mellitus. One of them was Benarous R *et al.,* 2011 [11]. Same finding was again seen in current study. In Group – I mean duration of diabetes was 13.15±5.8 years and in Group – II was 9.5±4.9 years (p = 0.001). Previously it was also established that raised HbA1c was associated with DR [12]. But in this study it was observed that not only DR, CSME was also associated with raised HbA1c (p =0.009). Similar finding was shown by Benarous R *et al.,* 2011. In this study level of all the components of fasting lipid profile were different between two groups. Mean TC level in Group – I (211.8 ± 54.8 mg/dl) was significantly different from Group – II (183.3 ± 44.5 mg/dl) (p = 0.019). This finding was similar to the finding of Jew OM *et al.,* 2012, a study done on Malayan people [13]. Miccoli R *et al.,* 1987, found mean serum cholesterol 212 mg/dl in exudative diabetic retinopathy patients which was similar to this study [14]. Dornan TL *et al.,* 1982, found high density lipoprotein (HDL) levels were similar in patients with and without retinopathy [15]. However in current study mean HDL was significantly lower in Group - I having CSME (p = 0.004) and though within normal range HDL level was border line in Group – II having no CSME. Regarding LDL cholesterol, different study showed different results. Kamoi K *et al.,* 2013 observed that there was no significant difference in means of HbA1c, TC, LDL and TC/HDL, between patients with and without clinically significant diabetic macular edema [16]. In contrast Benarous R *et al.,* 2011 found significantly higher LDL cholesterol in CSME patients than in those without CSME [17]. However in this study the mean LDL level in Group – I was (141.6±42.6 mg/dl) significantly higher than Group – II (118.5±26.7 mg/dl). In this study mean TG was 207±108 mg/dl in Group – I and 143.5±58.1 mg/dl in Group – II. Like TC and LDL, this study also showed the association of high level of TG in CSME patients (p = 0.003). In India Javadekar SD *et al.,* 2013, searched and found that TG and LDL were more deranged in CSME [18] which was similar as current study. In this study it was found significant association of dyslipidemia (at least one of the component was abnormal) & Diabetic retinopathy with CSME (88.9%) as well as without CSME (51.4%) (p = 0.001). Similar results were seen in ETDRS and WESDR studies [19]. In Group – I all the patients (100%) had hard exudate but in those of Group – II, 14 (40%) patients had hard exudate and rest 21 (60%) patients had no hard exudate. Patients who had hard exudate had their mean TC (total cholesterol) was 211.83±54.76 mg/dl, HDL was 35.78±6.4 mg/dl, TC/HDL ratio 6.04±1.63, LDL was 141.56±42.56 mg/dl and TG was 206±108 mg/dl and those who had no hard exudate their mean TC was 171.43±42.13 mg/dl, HDL was 41.86±8.41 mg/dl, TC/HDL ratio 4.12±1.19 mg/dl, LDL was 116.14±20.12 mg/dl and TG was 162.05±61.15 mg/dl. For all the components of lipid profile difference was significant (<0 .05). Similar finding was found in a study where it was concluded that elevated serum lipid levels are associated with an increased risk of retinal hard exudate in persons with diabetic retinopathy [17]. In another study hard exudate found to have statistically significant correlation with the presence of dyslipidemia, increased total cholesterol and LDL levels [16]. In a study done on African Americans Type – I diabetic patients, it was revealed that TC/HDL ratio of 4.5 or more were also at higher risk of having macular edema than those with a ratio less than 4.5 [20] which was also similar to this study.

CONCLUSION

Dyslipidemia is more common and its components are more deranged in Diabetic Retinopathy (DR) patients with CSME (Clinically Significant Macular Edema) than those without CSME. Findings also suggest that dyslipidemia have some effect on development of CSME in Diabetic Retinopathy patients in Type – II DM.

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