Scholars Academic Journal of Biosciences (SAJB) **ISSN 2321-6883 (Online)**
Sch. Acad. J. Biosci., 2015; 3(8):698-702 **ISSN 2347-9515 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com **DOI :** 10.36347/sajb.2015.v03i08.011

Research Article

Metabolic syndrome in patients with diabetes mellitus type 2 and its relation with retinal microvascular complication (diabetic retinopathy)

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Abstract: To find out frequency of MS and its components in type 2 DM cases and to evaluate its relation with retinal microvascular complication (diabetic retinopathy, DR). In this study 300 cases of Type 2 DM were recruited. The grading of the severity of DR and diagnosis of CSME was done using ETDRS protocol. MS was defined using modified NCEP ATP III criteria. MS was found in 180/300 (60%) cases. Subjects with MS had statistically significant higher BMI, wider WC, higher TG and high frequency of HTN ($p < 0.05$ for each). DR was found in 45% cases of MS and CSME was found in 21.70% cases. The MS was not significantly associated with DR or CSME in this study ($p > 0.05$ for each). The frequency of DR among patients having >10 years duration of DM was higher (53/56, 94.62%) than patients with < 10 year duration of DM (84/244, 34.43%). But in patients of MS having DM duration <10 years, frequency of DR (49/146, 33.6%) was not different than patients without MS. Also in MS patients with DM duration >10 years, frequency of DR (32/34, 94.1%) was not different from patients without MS ($p > 0.05$ for each). The independent risk factor for DR were glycated hemoglobin (OR 6.2019, 95% CI 3.7179-10.3456, $p < 0.0001$) and hypertriglyceridemia (OR 3.4983, 95% CI 1.9949-6.1344, $p < 0.0001$). MS was highly frequent (60%) among DM cases. It was significantly associated with female gender, obesity, higher TG and HTN. The independent risk factors for DR were hypertriglyceridemia and glycosylated hemoglobin.
Keywords: Metabolic Syndrome, Diabetes mellitus, Diabetic Retinopathy

INTRODUCTION

Metabolic syndrome (MS) consists of a cluster of diseases including central obesity, dyslipidemia, and hypertension and insulin resistance. MS is associated with a high risk of cardiovascular disease (CVD) and premature mortality [1]. Insulin resistance is a characteristic feature of Type 2 diabetes mellitus (type 2 DM). MS is highly prevalent among diabetics. Nearly 70-80% of the population with DM is diagnosed with MS [2-4]. MS can results in both macrovascular and microvascular complications in patients with type 2 diabetes mellitus as reported in previous studies [5-7]. The link between MS and DM may be due to negative cross talk between angiotensin II and insulin signaling [8].

The present study aims to find out the frequency of MS and its components in type 2 DM cases and to evaluate its influence on retinal microvascular complication (diabetic retinopathy, DR).

MATERIAL AND METHODS

This was a hospital based analytic study done in upgraded department of Ophthalmology at a tertiary care centre in Rajasthan among 300 cases of Type 2 DM (defined as per ADA 2007criteria)[9] who visited retina clinic and ophthalmology outdoor during September 2011 to September 2012. All patients gave their written consent before enrolling in the study. Cases of DM who had pregnancy, accelerated hypertension, active systemic infection, coexisting ocular disorders like uveitis, opaque/hazy media, retinal disorders like retinal vein/artery occlusions, retinitis pigmentosa, vitreoretinal degenerations and dystrophies, high myopia and recent ocular surgeries (<6 months) including vitreo-retinal surgery for causes other than DR, neovascular glaucoma or neovascularization of Iris were excluded from the study.

After taking complete history, a detailed physical and ophthalmic evaluation was done among all the subjects. Best-corrected visual acuity (BCVA) for distance according to ETDRS protocol and for near using Jaeger's chart were noted. The optic disc, macula and the retinal background were evaluated using indirect ophthalmoscopy and slit-lamp biomicroscopy with 78 diopter (D) lens, fundus photographs and fluorescent fundus angiography. Laboratory

investigation- ECG, Haemoglobin, fasting and 2 hour postprandial blood sugars, glycated hemoglobin (HbA1c) and lipid profile were done.

The grading of the severity of DR and diagnosis of CSME was done using ETDRS protocol [10]. Blood sugar was measured by glucose oxidase technique on automated analyser. Glycated Hb (HbA1c) was measured by chromatography analyzer. Plasma lipoproteins were measured with glucose oxidase technique on automated analyser.

MS was defined using modified NCEP ATP III criteria [11] as having three or more of the following

- waist circumference ≥ 90 cm for males and ≥ 80 for females
- systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥85 mm of Hg (or on treatment for hypertension)
- serum triglyceride levels ≥ 150 mg/dl
- serum HDL cholesterol < 40 mg/dl for male and <50 mg/dl for females
- Fasting blood sugar ≥ 100 mg/dl (or on treatment for diabetes mellitus). As all study participant were diabetic so patients of DM with two or more of the above criteria were diagnosed as having MS.

STATISTICAL ANALYSIS

Microsoft Excel and SPSS 17.0 for Windows were used for data storage and analysis. Continuous variables were expressed as mean ± standard deviation. Multivariate logistic regression analyses were performed to elucidate the risk factors for DR. The Odds Ratio (OR), with 95% confidence intervals, was calculated for the studied variables. Statistical significance was set at P value ≤ 0.05

OBSERVATIONS

The study population included 300 patients of DM type 2 (166 male and 134 female) with mean age 60.68 ± 9.43 years (age range 42-80 years), mean duration of disease was 75.39 ± 63.88 months (range 12-300 months). Metabolic syndrome was found in 180/300 (60%) cases. One hundred sixteen female and 64 male patients had metabolic syndrome. The MS was more common in female patients. Subjects with MS had statistically significant higher BMI, wider WC, higher TG and high frequency of HTN (p <0.05 for each). While no significant difference was found for age, duration of DM, Hb, glycated Hb, FBS, TC, LDL and HDL levels among both groups (P >0.05 for each). HTN was found in significantly higher number of MS cases (90/180, 50%) compared to cases without MS (17/120, 14.20%) (p<0.0001). While no significant difference was observed for occurrence of higher WC (100/180, 55.60% v/s 68/120, 56.70%), elevated TG (44/180, 24.40% v/s 68/120, 56.70%) and reduced HDL (84/180, 46.70% v/s 55/120, 45.80%) among MS and cases without MS. (p >0.05). (Table -1)

Table-1: Characteristics of the study subjects

	Metabolic syndrome		Total (300)	P
	Present (180)	Absent (120)		
Age (years)	60.09 ± 9.43	61.56 ± 9.40	60.68± 9.43	>0.05
Female (n)	116	18	134 (44.67)	<0.05
Male (n)	64	102	166 (55.33)	
Duration of DM (months)	75.63 ± 65.15	75.03 ± 62.20	75.39 ± 63.88	>0.05
Hb (gm/dl)	16.03 ± 6.57	11.94 ± 1.86	14.39 ± 51.57	>0.05
HbA_1C (%)	6.98 ± 1.22	6.96 ± 1.17	6.97 ± 1.19	>0.05
FBS (mg/dl)	130.18 ± 36.71	131.39 ± 35.27	130.66 ± 36.09	>0.05
BMI (kg/m^2)	24.95 ± 2.90	23.02 ± 2.09	24.18 ± 2.78	0.0001
WC (cm)	88.18 ± 8.37	80.74 ± 8.92	85.20 ± 9.32	0.0001
TC (mg/dl)	169.64 ± 41.42	160.90 ± 36.31	166.15± 39.63	>0.05
LDL(mg/dl)	104.78 ± 31.73	102.44 ± 28.16	103.85 ± 30.32	>0.05
HDL(mg/dl)	43.94 ± 5.23	44.79 ± 4.01	44.28 ± 4.79	>0.05
TG(mg/dl)	143.53 ± 53.50	113.98 ± 29.59	131.71 ± 47.67	0.0001
HTN(n)	90 (50.00)	17 (14.20)	107 (36.33)	0.0001
Increases WC(n)	100 (55.60)	68 (56.70)	168 (56)	>0.05
Elevated TG(n)	44 (24.40)	29 (24.20)	73 (24.33)	>0.05
Reduced HDL(n)	84 (46.70)	55 (45.80)	139 (46.33)	>0.05
DR(n)	81 (45.00)	56 (46.70)	137 (45.67)	>0.05
CSME(n)	39 (21.70)	25 (20.80)	64 (21.30)	>0.05

In subjects with DM, with or without MS, DR was found in 45% and 46.70%, CSME in 21.70% and 20.80% cases respectively. The MS was not significantly associated with the retinal microvascular complications (DR, CSME) (p>0.05 for each). (Table-1)

The frequency of DR among patients having >10 years duration of DM was higher (53/56, 94.62%) than patients with < 10 year duration of DM (84/244, 34.43%). But in patients of MS having DM duration <10 years, frequency of DR (49/146, 33.6%) was not different than patients without MS. Also in MS patients with DM duration >10 years, frequency of DR (32/34, 94.1%) was not different from patients without MS. (p>0.05 for each) (table no. 2)

To evaluate the relation between the presence of diabetic retinopathy and individual MS components, a multiple logistic regression analysis by adjusting variables such as age, gender was performed. It showed that the independent risk factor for DR were glycated hemoglobin (OR 6.2019, 95% CI 3.7179-10.3456 , p < 0.0001) and hypertriglyceridemia (OR 3.4983, 95% CI 1.9949-6.1344, p <0.0001) (Table-3).

Table-2: Association of Metabolic syndrome, duration of DM and diabetic retinopathy

Duration 0- 10 years		Metabolic syndrome		P >0.05
		Present(146)	Absent(98)	
	DR 84(34.43)	49(33.6)	35(35.7)	
Duration >10 years		Metabolic syndrome		P >0.05
		Present(34)	Absent(22)	
	DR 53(94.62)	32(94.1)	21(95.5)	

Table-3: Multiple logistic regression analysis for risk factors of DR (age and sex matched)

	DR		OR	95% CI	P
	Absent (163)	Present (137)			
Increased BMI	98(60.12)	88(64.23)	1.1912	0.7449-1.9048	0.4651
Increased WC	88 (54.0)	80(58.4)	1.1962	0.7562-0.8921	>0.05
Hypertriglyceridemia	23(14.11)	50(36.50)	3.4983	1.9949-6.1344	<0.0001
Low HDL	83(50.92)	56(40.88)	0.6664	0.4212-1.0541	0.0828
HTN	54(33.13)	53(38.67)	1.2736	0.7929-2.0457	0.3172
Elevated HbA_1C	34(20.86)	85(62.03)	6.2019	3.7179-10.3456	<0.0001

DISCUSSION

In modern era, sedentary life style had leads to emergence of metabolic syndrome as a common health problem. This study was conducted to find frequency of MS in cases of DM type 2 and to assess relation of retinal microvascular complications (DR) with individual MS component.

In this study MS was found in 180/300 (60%) of DM cases. Previous studies had reported 69.5-79.7% prevalence of MS among diabetic patients [7, 12-16]. Since this study was done among DM cases, one component of MS (FBS>100 mg/dl) was present in all cases. Therefore the MS in this study was not the same as in general population.

The MS was more common in female patients in this study (116 vs 64). Only Shimajiri et al. [17] found higher prevalence in men. Indian studies [12,18] and others [13-15] also observed higher prevalence of MS in women. Benadonna et al. [7] also had similar finding and they commented in their study that this trend could be due to a true biological phenomenon or a suboptimal choice of gender specific diagnostic threshold of taking lower cut-off for waist circumference and higher cut-off for HDL in women.

Significant association of MS with higher BMI, increased WC, raised TG and hypertension as observed in this study, was also concluded by Benadonna et al. [7].

The association between MS and microvascular complications of DM (DR, CSME) was not significant in this study. Iwasaki et al [13] and Ramanet et al [18] also did not show any significant association of MS with the prevalence of DR. In contrast, studies on population other than Asian, [5,7,17,19] have reported association of MS with microvascular complications of DM. This might be due to possible ethnicity related differences.

In this study, in cases of MS in addition to DM; four risk factors were present in 12 (6.67%), three risk factors in 46 (25.56%), two risk factors in 122 (67.68%) and one risk factor in 59 (32.78%) cases. Surana et al. [12] observed that among MS cases, 19.04% were positive for all five risk factors, 36.35% had four risk factors, and 44.6% had three risk factors.

In this study after DM and increased WC, HTN (90 cases, 50%) was the most frequent risk factor

followed by reduced HDL (84 cases, 46.70%) and hypertriglyceridemia (44 cases, 24.40%). Surana et al. [12] also found obesity as the most frequent component of MS, followed by HTN and elevated TG.

This study also observed decrease in frequency of MS along with increase in duration of DM, a finding similar to Ghani et al[19]. A plausible explanation for the same might be that all our patients were on drugs and their DM was well controlled (HbA1C 6.97 ± 1.19%). Shimajiri et al. [17] also reported that the prevalence of MS decreases along with an increase in the duration of diabetes. They suggested the possible reason to be a decreased BMI as a result of medical intervention in the lifestyle of long term diabetic patients.

The association between MS and DR was not significant in this study. Iwasaki et al. [13] and Raman et al. [17] also did not show any significant association of MS with the prevalence of DR.

We found elevated TG and high HbA1C as significant risk factors for DR. These associations have also been reported in previous studies [1,5,18,20].

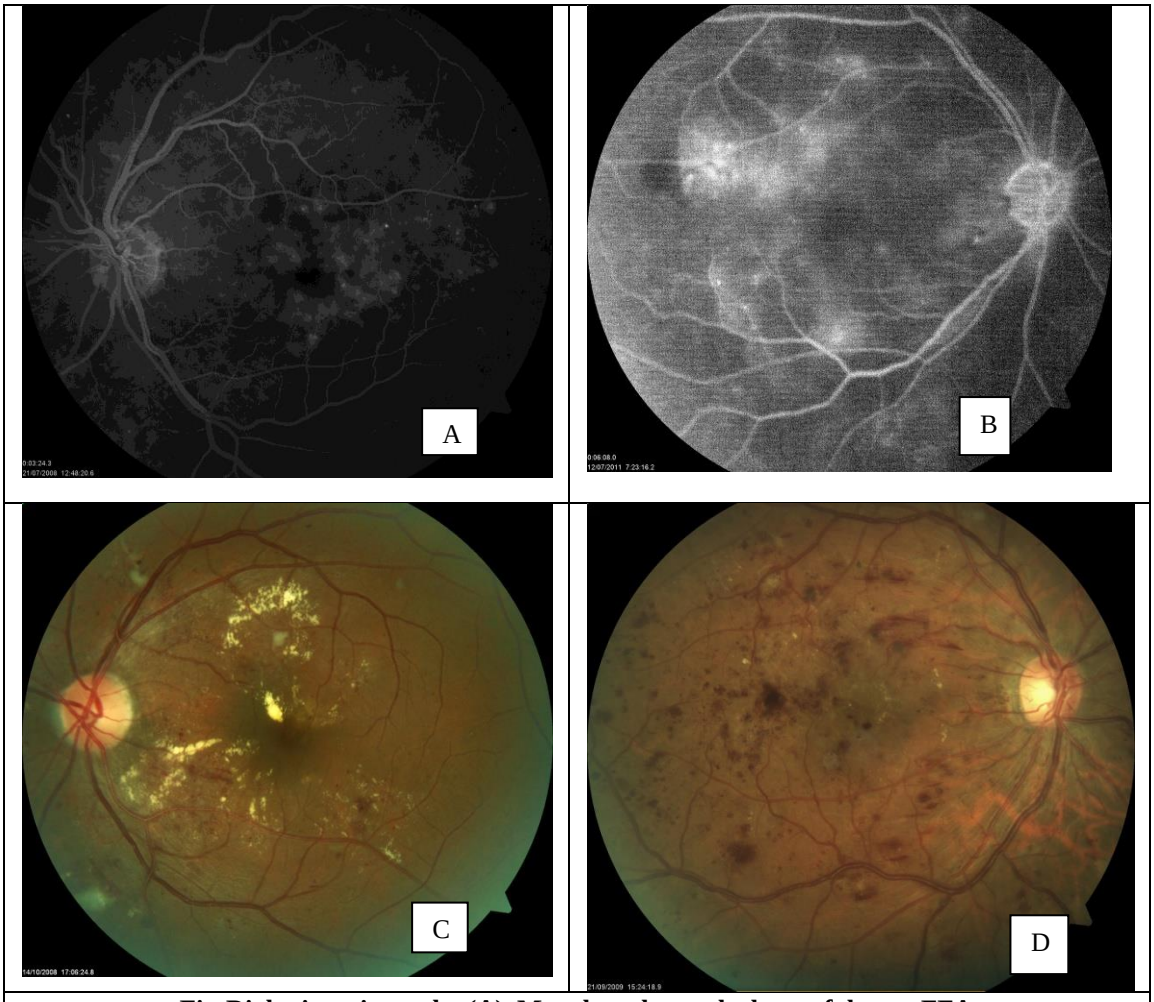

Fig-Diabetic retinopathy (A). Maculae edema : leakage of dye on FFA
(B) Proliferative diabetic retinopathy on FFA (C) Fundus photograph showing CSME
(D) Fundus photograph showing proliferative diabetic retinopathy

CONCLUSION

MS was highly frequent (60%) among DM cases. It was significantly associated with female gender, obesity, higher TG and HTN. The independent risk factors for DR were hypertriglyceridemia and glycosylated hemoglobin.

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