The Relationship between Diabetic Retinopathy and Metabolic Syndrome in Type 2 Diabetes Mellitus

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ABSTRACT:

BACKGROUND:

Diabetic retinopathy (DR) is the leading cause of blindness in both the developing and developed countries.The "metabolic syndrome" (MetS) is the clustering of abdominal obesity, insulin resistance, dyslipidemia, and elevated blood pressure and is associated with other comorbiditiesincluding the prothrombotic, and proinflammatory state, MetSis clearly associated with macrovascular complications, but its association with microvascular disease as retinopathy is unclear.

OBJECTIVE:

To find out the possible association between DR and MetS.

SUBJECTS AND METHOD:

Four hundred thirty one diabetic patients fulfilling the inclusion criteria were selected for this study The metabolic syndrome was definedfollowing the national cholesterol education program-Adult. treatment panel III guidelines.the ophthalmologic examinations wereperformedbyophthalmologiststoconfirmorexcluderetinopathy.Height,weight,waist circumference and blood pressure were obtained from all participants. Fasting venous blood samples were collected from all the subjects, HbA1c was estimated by high performance liquid chromatography,the serum wasused for analyzing Fasting Blood Glucose (FBG), Total cholesterol (TC), HDL-cholesterol (HDL-C) andTriglycerides (TG).

Statisticalanalysis of data was performed using statistically package for social science (SPSS) version 17.0

RESULTS:

The DR prevalence differedsignificantlybetween diabetics with and without metabolic syndrome (20.8% vs. 6.08%)the prevalence of metabolic syndrome in the whole studied sample was 72.6 %. Diabetics with DR hadsignificantlylonger duration of diabetes, had wider WC,higherFBG,higher HbA_{1c},higher systolic BP,are more likelyto be female,older, have a higher prevalence of MetS, and nonsignificant lower HDL-C and TG.Patients with concomitant MetSand DR hadsignificantly higher FBG, HbA_1C, SBP, TG, WC and lower HDL than diabetics with MetS but without DR.theprevalence of DR increased as the numbers of metabolic syndrome components increased.

CONCLUSION:

Diabetic subjects with metabolic syndrome are at higher risk to develop retinopathy. The prevalence of DR increased as the numbers of metabolic syndrome components increased.

KEYWORDS: diabetic retinopathy, metabolic syndrome, type 2 diabetesmellitus.

INTRODUCTION:

Diabetes mellitus is a chronic illness that requires continuing medical careand ongoing patient education and support to prevent acute complicationsand to reduce the risk of long-term complications, diabetes care iscomplex and requires that many issues, beyondglycemic control, be addressed[(1)] TheWorld Health Organization has estimated that the number of adults with diabetes in the world would increase alarmingly from 135 million in 1995 to 300 million by 2025[(2)].

Diabetic retinopathy is the leading cause of blindness in both the developing and developed countries;it may begin to develop as early as 7 years before the diagnosis of diabetes in patients with type 2 diabetes [(3)].Diabetic retinopathy involves occlusion and leakage of retinal vessels, leading to macular edema in the nonproliferative phase and angiogenesis and to tufts of highly permeable vessels in the proliferative phase.

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Macular edema remains the clinical feature most closely associated with vision loss, and thickening of the central fovea [4].Vision loss due to DR occurs through a variety of mechanisms, including retinal detachment, preretinal or vitreous hemorrhage, associated neovascular glaucoma, and macular edema or capillary nonperfusion[5]

The "metabolic syndrome" (MetS) is the clustering ofabdominal obesity, insulin resistance, dyslipidemia, and elevatedblood pressure and is associated with other comorbiditiesincluding the prothrombotic state, proinflammatorystate, nonalcoholic fatty liver disease, and reproductive disorders, The MetS has also been shown to be associated with an increased risk of chronic kidney disease [6],microalbuminuria[7]and with increased risk for neuropathy [8]. The prevalence of the MetS isincreasing to epidemic proportions, and theclustering of itscomponents reflect overnutrition, sedentary lifestyles, and resultant excess adiposity.Abdominal adiposity and insulin resistance appear to bethe core of thepathophysiology of the MetS and its individual components[9].The MetS is clearly associated with macrovascular complications as coronary heart diseases, but its association with microvascular disease as retinopathy is unclear [10], as there is growing evidence that MetS, like diabetes mellitus, causes microvascular complications in patients with type 2 diabetes mellitus [11,12].

OBJECTIVE:

To find out the possible association between DR and MetS

SUBJECTS AND METHODS:

A total of fivehundred diabetic patients participate in this study who attended the National Diabetic Center, Al-Mustansiria University.

- Inclusion criteria:type 2 diabetic subjects with and without the MetS.
- Exclusion criteria:Smokers, pregnant women, patients with type I diabetes, subjects with advanced renal, cardiac or liver disease or patients on certain medication that affect the tested parameters were excluded from the study, sixtynine(69) were excluded ,the remaining were four hundred thirty one(431) ,their mean age was 55.6 ± 9.3 years , 207(48.02%)male and 224(51.9 %) were female.

Definition of Metabolic syndrome:

The metabolic syndrome was definedfollowing the National Cholesterol Education Program - Adult Treatment Panel III guidelines[13]as meeting at least three of the following five criteria: (a) abdominal obesity (waist circumference >102 cm in men, >88 cm in women), (b) triglyceride level ≥150 mg/dL (c) low HDL cholesterol (<40 mg/dL in men, <50 mg/dL in women), (d) systolic blood pressure ≥130 mm Hg and/or diastolic blood pressure ≥85 mm Hg or using antihypertensive medication, and (e) high fasting glucose (≥110 mg/dL or using antidiabetic medication). Lipid and blood glucose levels were measured after an overnight fast. Height, weight were measured andBMI was calculated as weight in kilograms divided by height in meters squared,waist circumference and blood pressure were both averaged over two measurements,waist circumferences were measured in a horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest.

Diabetic Retinopathy:

The ophthalmologic examinations were performed by ophthalmologists to confirm or exclude the presence of retinopathy,DR was defined as the presence of 1 or more retinal microaneurysms or retinal blot hemorrhages with or without more severe lesions (hard exudates, cotton wool spots, intraretinalmicrovascular abnormalities, venous beading, retinal new vessels, preretinal and vitreous hemorrhage, and fibroproliferans) using the Early Treatment Diabetic Retinopathy Study (ETDRS) grading standards[14].

Analytical Methods:

Fasting venous blood samples were collected from all the subjects,blood was drawn from the antecubital veinof seated participants and serum wasused.HbA1c was estimated by high performance liquid chromatography (supplied by Variant Company, USA),value of HbA1c was given as percentage of total hemoglobin,the serum was used for analyzing Fasting Blood Glucose , Total cholesterol , HDL-cholesterol, Triglycerides (all were measuredspectrophotometrically),Glucose level was determined using kits supplied by Randox, UK, total cholesterol, triglycerides, high density lipoprotein were determined using kits (Biomaghrab,Sa,France),

Statistical analysis: Analysis of data was performed using statistically package for social science (SPSS) version 17.0. Results are expressed as mean ± SD,Student ttest was used to compare the significance of the difference in the mean values of any two groups and chi

square analysis was used to compare frequency between two groups, P<0.05 was considered statistically significant.A logistic regression model wasused to examine the independent association between DR and metabolic syndromecomponents and other related factors.

RESULTS:

DR prevalence differssignificantlybetween diabetics with and without MetS (20.8% *Vs* 6.08%, P=0.000).

The prevalence of metabolic syndrome in the studied population was 72.6 %. (n=327)no gender difference were observed (male=163, 48 %.female =164, 52% P=0.9)

Table 1 shows characteristics of the participants by DR status,the diabetics withretinopathyhave higher prevalence of MetS, were more likely (statistically significant) to be older, withlonger duration of diabetes, female, have wider WC,higherFBG,higher HbA_{1c},higher systolic BP,and nonsignificant lower HDL-C and TG than patient without DR.

Table2 showed statistically significant difference in the prevalence of DR between patients with and without MetS.

Patients with MetS who develop DR have statistically significant higher FBG, HbA_{1C}, SBP,TG, WC (in male) and lower HDL-C as shown in table 3.

the prevalence of individual components of metabolic syndrome were 72.2% for abdominal obesity, 34% for elevated triglycerides, 64.4 % for low HDL-C, 82.2% for hypertension(table 4)

The effect of clustering ofMetScomponents on the prevalence of DR is shown in table5.

logistic regression analysis (shown in table 6) between DR and MetS components and some other factors demonstrated that age ,SBP, waist circumference, ,BMI,diabetic duration, HbA_{1c} and the number of MetS components are independent factors associated with DR.

Table 1: Baseline, demographic and biochemical characteristics of the diabetics with and without retinopathy.

	Diabetic with retinopathy	Diabetic without retinopathy	p-value
Number (%)	73(16.9%)	358(83.06%)	
Gender (male:female)	30:43	168:190	
Age (years)	60.22± 8.4	54.55±9.3	0.000**
Diabetic duration(years)	11.8±2	7.06±1.5	0.000**
Fasting blood glucose(mg/dl)	204± 10	184± 9	0.03*
HbA_{1c} (%)	9.3 ± 1.9	8.7± 2.1	0.02*
Waist circumference(cm) male female	101±9.3 104±10.3	99±9.8 100±10.6	0.2 0.03*
BMI(kg/m^2)	30.8 ± 4	29±3.2	0.06
Systolic blood pressure(mmHg)	149.8 ± 20	135.5±15	0.000**
Diastolic blood pressure(mmHg)	87.1± 11	86.1± 10	0.4
Serum total Cholesterol (mg/dL)	173±10	177± 12	0.5
Serum triglyceride (mg/dL)	145± 11	149± 13	0.6
HDL-C (mg/dL)	44±3	45± 2	0.2
Prevalence of metabolic syndrome (%)	66 (90.4%)	250(69.8%)	0.000**

Results are expressed as mean ± SD,P value less than 0.05 is considered statistically significant*, P value less than 0.001 is highly significant**

Table2: The difference in the prevalence of DR in patients with and without MetS.

	Diabetic without MetS	Diabetic with MetS	P-value
Number	115	316	
Prevalence of Retinopathy n (%)	7(6.08%)	66 (20.9 %)	0.000

Table 3: Characteristics of patients with metabolic syndrome according to the presence or absence of diabetic retinopathy.

	MetSwithout Diabetic retinopathy	MetSwith Diabetic retinopathy	P-value
Age (years)	54.5 ±9.3	60.3± 4.8	0.000**
Diabetic duration(years)	7.06 ± 1.9	9.8 ± 2	0.06
Fasting blood sugar(mg/dl)	184 ± 3.8	204 ±9.4	0.03*
HbA_{1c} (%)	8.7±2.1	9.3±1.9	0.02*
Waist circumference(cm)male female	90±8 97± 9.8	104 ±7 105±9.3	0.001** 0.01*
BMI(kg/m^2)	30.6±4.2	31.2±5.5	0.4
Systolic blood pressure(mmHg)	135.5 ±19.2	149.8±21	0.000**
Diastolic blood pressure(mmHg)	86±10	87±11	0.61
TC (mg/dL)	149.5±19	144.8±13	0.607
TG (mg/dL)	90.2±4.8	150.6±8.8	0.000**
HDL (mg/dL)	47.3 ± 3	44.9 ±2	0.05*

Results are expressed as mean ± SD,P value less than 0.05 is considered statistically significant*,if P value less than 0.001 it is highly significant**

Table 4: Prevalence of metabolic syndrome components in diabetic retinopathy (P-value between male and female).

	Number (%)	male	female	P-value
Hypertension	60 (82.2 %)	23(38.3%)	37(61.6%)	0.3
Increased WC	52 (72.2 %)	13(25%)	39(75%)	0.000**
Hypertriglycerdemia	21 (34 %)	7(33.3%)	14(66.6%)	0.07
Reduced HDL -C	38 (64.4 %)	16(42.1%)	22(57.8%)	0.9

Table5: The effect of clustering of MetScomponents on the prevalence of DR.

NO. of MetS components	Total NO. Of patients	NO. of patients without diabetic retinopathy	NO. of patients with diabetic retinopathy	Percentage
One component	31	30	1	3.2 %
two components	88	81	7	7.9 %
Three components	169	137	32	18.9%
Four components	108	84	24	22.2 %
five components	35	26	9	25.7 %

Table 6: logistic regression analysis between DRand the MetS componentsand some other factors(DR is the dependantvariable, P less than 0.05 is statistically significant *and if P less than 0.001 it is highly significant

	Odd ratio	95% Confidence interval		P-value
		Lower	upper	
DM duration(years)	0.950	0.901	1.002	0.050*
HbA_{1c} (%)	0.862	0.743	0.999	0.048*
SBP(mmhg)	0.973	0.957	0.989	0.001**
DBP(mmhg)	1.003	0.966	1.041	0.888
TG (mg/dL)	0.998	0.992	1.005	0.617
HDL(mg/dL)	0.916	0.805	1.043	0.188
Waist (cm)	1.061	0.994	1.133	0.046*
Age (years)	0.963	0.928	0.999	0.046*
BMI (kg/m^2)	0.817	0.719	0.929	0.001**
Metabolic componentsno.	1.556	1.201	2.016	0.001**

DISCUSSION:

Metabolic syndrome (MetS) is an important public health problem worldwide, and its prevalence is increasing, insulin resistance appears to underlie this syndrome [14].Patients with MetS are at higher risk for many long-term complications; this is particularly relevant in patients with type 2 diabetes mellitus (T2DM), who are at even greater risk [15].

the prevalence of MetS in the studied population was 72.6%, this prevalence is much higher than the values reported in general populations [16,17] and similar to the studies on T2DM from other diabetic populations [18,19]. Using the Third Report of the National Cholesterol Education Program Adult Treatment Panel definition; over 65% of patients with T2DM have MetS[20]

This study revealed that diabetics with retinopathy had statistically significant higher FBG, HbA_{1C}, higher SBP , longer duration of DM, and with higher prevalence of MetS (90.4% *vs*69.9% P=0.000) ,these findings are in agreement with other studies that found that hyperglycemia [21] , hypertension [21,22] and DM duration [21,23] are important risk factors for DR develoment . however evidence from large epidemiological trials such as (ADVANCE)3 had shown a limit to the risk reduction for DR that can be achieved with better glucose and blood pressure management alone[24],suggesting that other risk factors (i.e. dyslipidemia, obesity, and inflammation) may explain the occurrence of DR [25]

The prevalence of DR in diabetics with MetSin this study was higher than its prevalence in diabetics without the MetS (20.8% *Vs* 6.08% P=0.000), comparable to that noted by other investigators [26], insulin resistance is thought to be an important risk factor for DR development, this is supported by the result of other studies that found that metabolic syndrome in non-diabetic subjects was found to be associated with high retinal microvascularrisk,similar to that observed in diabetic retinopathy[25]

The present study showed that diabetics with retinopathy had wider waist circumference than those without retinopathy, this can be explained by the fact that central obesity, is associated with endothelial dysfunction due to abnormality in the generation and release of endothelial derived nitric oxide, which had central role in the maintenance of vascular tone, platelet adhesiveness and smooth muscle cell proliferation[27] .In addition obesity may increase oxidative stress by its associated hyperleptinemia that participate in DR development [28]the relationship between obesity and increased risk of retinopathy had been documented by other studies [29].

Patients with concomitant MetS and DR have significantly higher serum TG and lower serum HDL-C level compared to diabetics with MetS but without DR. dyslipidemia may cause the development and progress of DR by increasing blood viscosity and altering the fibrinolytic system [30]in addition the atherogenic dyslipidemia up-regulate the inflammatory adipokine, tumor necrosis factor α, interleukin 6, and C-reactive protein [18], this chronic subclinical inflammation of the MetS play an important role in the development of microvascular complications as retinopathy [31].

The study revealed that DR prevalence increased as the numbers of metabolic syndrome components increased, in agreement with some studies that reported an increase in the prevalence of microangiopathies when patients were grouped according to the number of MS components [10]

CONCLUSION:

Diabetic subjects with metabolic syndrome are at higher risk to develop retinopathy than diabetic subjects without the syndrome. The prevalence of DR increased as the numbers of metabolic syndrome components increased.

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