Diabetic Retinopathy Predicts In-Hospital Outcome of

Coronary Artery Disease

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اعتلال الشبكية السكري يتنبأ بمصير مرض الشريان التاجي خلال فترة الرقود في المستشفى

الخلاصة: خلفية الموضوع: مرض الشريان التاجي و اعتلال الشبكية السكري كلاهما من الاختلاطات المعروفة لمرض البول السكري. <u>الهدف</u> هو دراسة العلاقة بين وجود اعتلال الشبكية السكري و حصول اختلاطات مرض الشريان التاجي في فترة رقود المريض في وحدة العناية القلبية. <u>المرضى والطرق:</u> خمسون مريضا بداء السكري من النوع الثاني تم اختيار هم من بين المرضى الراقدين في وحدة العناية القلبية في مستشفى الصدر التعليمي في النجف، ستة و عشرون منهم لديهم دلائل اعتلال الشبكية السكري مقابل أربعة و عشرين ليس لديهم هكذا دلائل. تم تتبع ظهور اختلاطات مرض الشريان التاجي عند العناية التنابع: من اصل ستة و عشرين ليس لديهم هذا دلائل. تم تنبع ظهور اختلاطات مرض الشريان التاجي عند الجميع. المتنابع: من اصل ستة و عشرين ليس لديهم هذا دلائل. تم تنبع ظهور اختلاطات مرض الشريان التاجي عند الجميع. المتنابع: من اصل ستة و عشرين ليس لديهم هذا دلائل. تم تنبع ظهور اختلاطات مرض الشريان التاجي عند الجميع. المتنابع: المرين السريان التاجي؛ مقابل عشرة مرضى من اصل أربعة و عشرين مريضا ليس لديهم دلائل اعتلال الشبكية السكري. هذه العلاقة ظهر بأنها مهمة إحصائيا (قيمة P اقل من مربر). الشبكية السكري. هذه العلاقة ظهر بأنها مهمة إحصائيا (قيمة P اقل من من).

Abstract:

Background: Coronary artery disease together with diabetic retinopathy is well known complications of diabetes mellitus (DM). **Our aim** is to study the correlation between the presence of diabetic retinopathy and the development of complications of coronary artery disease in the period of admission to the coronary care unit. **Patients & method:** Fifty patients with DM II were selected from coronary care unit attendants at Assadr Teaching Hospital in Najaf; 26 with evidence of diabetic retinopathy vs. 24 without. All were followed up for occurrence of complications of coronary artery disease. **Results:** Eighteen Out of the 26 patients with diabetic retinopathy developed complications of coronary artery disease vs. 10 out of the 24 patients without diabetic retinopathy; an association which appeared to be statistically significant (P value <0.05). **Conclusion** Diabetic retinopathy has significant association with, and can be used as predictor of, the occurrence of coronary artery disease complications during the period of admission to the coronary care unit.

Introduction:

Diabetes mellitus causes well-known micro- & macroangiopathic complications; coronary artery disease & diabetic retinopathy are well-known examples. These two complications were studied extensively; each alone & in combination or in association with other types of complications; to predict, better manage, and to prevent them if possible 1, 2, 3.

Diabetic retinopathy is an early frequent marker of other cardiovascular complications, and people with diabetes mellitus have greater risk of premature morbidity & mortality due to cardiovascular disease than general population & cardiovascular disease accounts for 75% of death in this population group^{1, 2, 3, 4,5,6,7}. The prevalence of diabetic retinopathy among diabetic population ranges from 20% to above 34%; with the lowest prevalence in those 80 years or more, and it is higher in blacks than in whites ^{2,3,4,5,6,7}Risk factors for diabetic retinopathy includes family history, diabetes mellitus duration > 5 years, systolic blood pressure > 125mmhg, smoking & hyperlipidemia^{5,8,9}.

On the other hand, coronary artery disease associated with diabetes mellitus is characterized by its particular severity which is essentially due to the severity of coronary atherosclerosis, which is usually multi-vessel, involves both large trunks and microcirculation, is made of frequently lipid-rich and therefore fragile plaques, and is accompanied by abnormal but specific reactions of the arterial wall (tendency to vasoconstriction and increased neointimal proliferation after trauma)¹⁰. Coronary atherosclerosis is also often associated with hypertension, lower limb arteriopathy or cerebral atherosclerosis¹⁰.

The aim of the study: In this study we try to evaluate the use of diabetic retinopathy; which is simple to detect by trained physicians; as a marker for predicting prognosis of coronary artery disease in coronary care unit attendants during their period of admission in order to pay more attention for the more risky group which is; in this study; postulated to be the group that has evidence of diabetic retinopathy.

Patients & methods:

The study was conducted in Assadr Teaching Hospital in Najaf over a period of six months, starting from August, 2006. The study group included 50 patients, 26 with evidences of diabetic retinopathy vs. 24 without such evidences who were taken as control . The patients were ranging from 40 - 75 years old with a mean of 57.48 year (SD \pm 7.8 yr.), and a male to female ratio of 0.78 (22 male and 28 female). Patients included are those who are admitted to the coronary care unit for their coronary artery disease (based on clinical & electrocardiographical findings) and who are having diabetes mellitus (based on World Health Organization (WHO) criteria for diagnosis of diabetes mellitus) of type 2¹.

The only cause of exclusion was a patient with any media opacity that obscures fundus details.

All patients were examined for evidences of diabetic retinopathy (& its grade if present –background, preproliferative, proliferative and maculopathy-¹¹) using direct and indirect opthalmoscopy and slit lamp biomicroscopy.

Thereafter, the patients were followed up in the ward along their admission period for occurrence of complications of their coronary artery disease using the clinical, electrocardiographical, radiological, & echocardiographical evaluations. The complications were recorded & classified into groups which include: recurrent anginal pain, hemodynamic complications, electrical complications, & death¹.

Other baseline parameters taken into consideration were:

- 1- Age & sex of the patients.
- 2- Duration of diabetes.
- 3- Type of treatment.
- 4- History of coronary artery disease & its duration.
- 5- Whether or not the patient is hypertensive.
- 6- Whether or not the patient is smoker.

The data were analyzed using Chi-square test with a level of significance (P value) being < 0.05

Results:

As shown in Table-1; 26 patients with diabetic retinopathy were compared to a control group (24 patients) without diabetic retinopathy. Types & numbers of subgroups of diabetic retinopathy are shown in Figure-1.

Fifty two percent of the total patients included have history of coronary artery disease, 54% of them have history of hypertension and 22% were smokers. Sixty six percent of the patients were on oral treatment for their diabetes mellitus, while only 16% of them were on insulin therapy and 18% on diet control only. As shown in Figure-2; the presence of evidence of diabetic retinopathy was steadily increasing with the duration of diabetes mellitus.

The coronary artery disease complications encountered in the study were: hypotension & pulmonary edema (hemodynamic complications), atrial fibrillation, bifasicular block, 3rd degree heart block (electrical complications), recurrent anginal pain, & lastly death. These complications were recorded in 28 patients of the entire study group; 18 in those with diabetic retinopathy (69.2 %), vs. 10 in those without diabetic retinopathy (41.7 %). These data revealed a statistically significant association between the occurrence of coronary artery disease complications & diabetic retinopathy, as shown in Table-2, Figure-3& -4.

None of the above parameters revealed a statistically significant association with the occurrence of coronary artery disease complications apart from the presence of diabetic retinopathy when we compared the group of patients who developed coronary artery disease complication vs. those who did not; as shown in Table-3.

The relationship between occurrence of coronary artery disease complications & the **grades** of diabetic retinopathy is shown in Figure-5, which was statistically not significant.

Patient	Patien		0,		Patien		0,		Т
criteria	ts with			ts	without			otal	
	diabetic			dial	betic				
	retinopathy			reti	nopathy				
Total	26				24				5
No.								0	
Age (yr)	_								
40 – 49	2	_	7		3		1		5
=0 =0		.7			4.4	2.5	_		•
50 – 59	11	• •	4		14	07	5	_	2
60 60	10	2.3	2		6	8.3	1	5	1
00 - 09	10	Q 5	3		0	5	4	6	T
> 70	3	0.5	1		1	5	1	U	Λ
<i>≥</i> 70	3	15	T		T	2	4		4
Sev		1.0				•2			
Male	13		5		9		7		2
101uit	10	0	•			7.5	U	2	-
Female	13	Ū	5		15		6	-	2
		0	-			2.5	-	8	
History	13				13				
of coronary		50				54.2	2	26	
artery									
disease									
History	14				13				
of		53.8	3			54.7	7	27	
hypertension									_
Smokin									
g	40		_		• •		0		•
Nonsmo	19	0.1	7		20	• •	8	0	3
ker	-	3.1	~			3.3	4	9	1
Smoker	7	()	2		4		l	1	I
Dunatio		0.9				0./		I	
Durauo n of DM (vr)									
-5	Δ		1		11		Δ		1
\ 3	-	54	T		11	58	-	5	T
5. ~10	4	J.T	1		8	2.0	7	0	1
5- 10	Т	5.4	T		0	3.3	J	2	1
10- <15	3	~ • •	1		3		1	-	6
	2	1.5	-		-	2.5	-		5

Table - 1. Baseline characteristics of the patients in the study group with diabetic retinopathy (26)vs. the control group without diabetic retinopathy (24)

15- <20	6	2	1	4	7
≥ 20	9	3.1 3	1	.2 4	1
		4.6		.2 0	
Treatm					
ent of					
diabetes					
mellitus					
Diet only	3	1	6	2	9
•		1.5		5	
Oral	17	6	16	6	3
antidiabetics		5.4		6.7 3	
Insulin	6	2	2	8	8
		3.1		.3	

 Table - 2. The correlation between the presence of diabetic retinopathy and the occurrence of complication of coronary artery disease during the in-hospital period

occurrence of complication of coronary artery	Patients with diabetic retinopathy (26)	Patients without diabetic retinopathy (24)	Total	P value
disease Yes	18	10	28	< 0.05
No	8	14	22	





BDR=Background Diabetic Retinopathy PPDR=Preproliferative Diabetic Retinopathy PDR= Proliferative Diabetic Retinopathy M=Maculopathy







Figure - 3. Shows the No. & percentages of complications of coronary artery disease in both groups of the study

CAD= coronary artery disease DR= diabetic retinopathy



Figure - 4. Shows the types & frequencies of occurrence of coronary artery disease complications in the study group

Table - 3. Comparison between the group that developed coronary artery disease complication & the group that was free of such complication

Criteria	No. of patients with CAD complications(2 8)	%	No. of patients without CAD complicatio ns (22)	%	Tota I	P value
Age (yr)						>0.0
40-49	2	7.1	3	13.6	5	5
50-59	14	50	11	50	25	
60-69	11	39.3	5	22.7	16	
≥ 70	1	3.6	3	13.6	4	
Sex						>0.0
Male	12	42.9	10	45.5	22	5
Female	16	57.1	12	54.5	28	
History of	14	50	12	54.5	26	>0.0
coronary						5
artery						
disease						
Hypertensi	16	57.1	11	50	27	>0.0
on						5

Treatment						>0.0
of DM						5
Diet only	5	17.9	4	18.2	9	
Oral	17	60.7	16	72.7	33	
antidiabetic						
S		24.4		0.1		
Insulin	6	21.4	2	9.1	8	
Smoking						>0.0
Nonsmoker	20	71.4	19	86.4	39	5
Current	8	28.6	3	13.6	11	
DM						>0.0
duration(yr						5
/5	7	25	8	36 /	15	
< 5	7 7	25	5	22.7	12	
$\frac{5}{10} - < 15$	/ 3	107	3	13.6	6	
15 - < 20	5	179	2	9 1	7	
>20	6	21.4	4	18.2	10	
Presence of	18	64.3	8	36.4	26	<0.0
Diabetic						5
retinopathy						

CAD = coronary artery disease DM = diabetes mellitus



Figure-5. Compares the group of patients with coronary artery disease complications vs. that without, in regard to the subtypes of DR (P value > 0.05).

CAD= coronary artery disease

DR= diabetic retinopathy

BDR= background diabetic retinopathy

PPDR= preproliferative diabetic retinopathy

PDR= proliferative diabetic retinopathy

Discussion:

The concept of the predictive value of diabetic retinopathy with regard to cardiovascular disease & its management is based on many other previous studies. Specifically speaking; diabetic retinopathy was found to predict mortality after percutaneous coronary intervention (PCI) in diabetic patients¹². Diabetic retinopathy has also been shown to be associated with increased cardiovascular mortality in diabetic patients, and was associated with a higher risk of perfusion defects in subjects with cardiac and non cardiac chest pain. Moreover it was shown that diabetic retinopathy is a useful marker for selecting patient in whom thallium scintigraphic screening is warranted¹³. One study has found that among diabetic patients who are suspected of having coronary artery disease; those with diabetic retinopathy have more diffuse & severe coronary atherosclerosis vs. those without diabetic retinopathy.²

In this study; apart from "duration of diabetes mellitus " and "occurrence of complications"; none of the parameters taken showed statistically significant association with diabetic retinopathy. So, we readjusted the patients according to whether or not they have coronary artery disease complications, to further reveal any possible operating factor; yet, none (even the duration of diabetes mellitus) revealed a statistically significant association with occurrence of coronary artery disease complications apart from presence of diabetic retinopathy (P value < 0.05).

Concerning the *grade* of diabetic retinopathy:

Klein R, et al found that it was not associated with coronary artery disease ⁷, although in diabetes mellitus type I, Sundell J, et al had found that background diabetic retinopathy is associated with impaired coronary vasoreactivity in young people if compared with nondiabetics¹². Moreover; diabetes mellitus patients with proiferative diabetic retinopathy were found to have lower coronary collateral scores than patients without diabetic retinopathy & that vascular endothelial growth factor (VEGF) level was significantly higher in proiferative diabetic retinopathy group than those without diabetic retinopathy, suggesting that diabetes mellitus has different action on retinal and coronary circulation¹³. Auni Juutilainen, et al , revealed that proiferative diabetic retinopathy in both sexes and background diabetic retinopathy in women predict cardiovascular disease and coronary heart disease death ¹⁴

In this study; we found no statistically significant association between the grade (severity) of diabetic retinopathy & the occurrence of coronary artery disease complications during the period of admission to the hospital. This finding need to be further evaluated with a larger number of patients with diabetic retinopathy of different types.

The hyperlipidemia was not assessed in our patients despite the fact that it is a risk factor for both diabetic retinopathy & coronary artery disease. This is because of the well-known fact that lipid profile is disturbed acutely with any stressful condition including coronary artery disease that is assessed in our patients, that is, it is not compatible with the short duration (in-hospital period) in which we are concerned.¹¹

As we stated above; smoking & hypertension are established risk factor for the development of diabetic retinopathy. The absence of the association between smoking & diabetic retinopathy in our research work may be explained by the small size of the study group and/or the bias due to the criteria of selecting a patient to be enrolled in the study.

The same reasons can be applied to the absence of relationship between diabetic retinopathy and hypertension in our study.

Conclusion: Presence of diabetic retinopathy can predict patients more liable to develop coronary artery disease complications during their hospital attendance independent of the grade of the diabetic retinopathy.

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