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Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Original Research Article

Association between diabetic retinopathy and diabetic nephropathy: A clinical study

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ARTICLE INFO

Article history:
Received 30-11-2021
Accepted 27-12-2021
Available online 31-03-2022

Keywords:
Albuminuria
Diabetic Retinopathy
Fundoscopy
Nephropathy

ABSTRACT

Background: Diabetes mellitus is a leading cause of blindness worldwide. The disease affects the generalized micro and macro vasculature of various structures. Retina, kidney and peripheral nerves are the major sites of micro vasculature involvement. Our study aims to find the correlation between diabetic retinopathy (DR) and diabetic nephropathy.

Materials and Methods: This non-randomized, prospective study was conducted at a tertiary care hospital in South India between November 2014 and May 2016. Study included 100 patients with diabetic nephropathy referred for fundoscopy from the nephrourology department, excluding those with hazy media enough to interfere with a detailed fundus examination and management. All subjects underwent complete ocular examination and systemic evaluation after obtaining informed consent. Visual acuity, fundoscopy by direct and indirect ophthalmoscope, fundus photography and optical coherence tomography were done as and when required. Blood investigations like fasting blood sugar, post prandial blood sugar, glycosylated haemoglobin, haemoglobin levels, serum creatinine and blood urea nitrogen, lipid profile, urine routine and 24-Hour urine albumin were recorded. DR was classified according to ETDRS classification and different grades were compared with grades of nephropathy and association was analysed statistically.

Results: There was significant association between fundal changes and albumin excretion in urine. Among subjects with massive albuminuria, 64.7% of them had proliferative DR (PDR). Among subjects with moderate albuminuria, majority had Moderate NPDR and subjects with microalbuminuria majority had normal fundus. There was a positive correlation between DR and total cholesterol.

Conclusion: The severity of DR correlates with severity of diabetic nephropathy.

1. Introduction

Diabetes mellitus is a widely prevalent disease and is one of the leading causes of blindness worldwide.[1,2] The disease affects the generalized micro vasculature and macro vasculature of various structures. It takes years for microvascular complications in diabetes mellitus (DM) such as diabetic retinopathy (DR) and diabetic nephropathy (DN) to develop. Since retinal and renal vessels are exposed to the diabetic milieu, it is assumed that progression of DR and diabetic nephropathy occurs at the same time. Early detection of diabetic retinopathy helps in preventing vision threatening complications. Our study aims to find the correlation between DR and diabetic nephropathy and the influence of other risk factors such as duration of diabetes and hypertension on diabetic retinopathy and diabetic nephropathy changes.[3]

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https://doi.org/10.18231/j.ijceo.2022.025

2. Methodology

This is a non-randomized, prospective study was conducted at a tertiary care hospital in South India between November 2014 and May 2016. After obtaining approval from the Institutional Ethics Committee, 100 patients with diabetic nephropathy referred from the Nephrourology Department of our hospital for fundoscopy were included in the study. Diabetic nephropathy was defined by presence of either microalbuminuria or macro-albuminuria, in the absence of uncontrolled hypertension, congestive cardiac failure (CCF) and active urinary tract infection (UTI). Patients with hazy media enough to interfere with a detailed fundus examination and management, patients with CCF, UTI or uncontrolled hypertension, retinal proliferative disorders were excluded from the study. After obtaining basic demographic data and a detailed history, all subjects underwent complete ocular examination and systemic evaluation. Visual acuity, fundoscopy by direct and indirect ophthalmoscope, fundus photography and optical coherence tomography were done as and when required. Blood investigations like fasting blood sugar, post prandial blood sugar, glycosylated haemoglobin, haemoglobin levels, serum creatinine and blood urea nitrogen, lipid profile, urine routine and 24-Hour urine albumin were recorded. DR was classified according to ETDRS classification and different grades were compared with grades of nephropathy and association was analysed statistically. Data was analyzed using SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) software and appropriate statistical tools.

3. Results

Majority of subjects were in the age group 41 to 50 years (33%), followed by 51 to 60 years (31%). Mean age of subjects in the study was 52.64 ± 10.57 years. (Table 1)

Table 1: Mean age of subjects in the study

		Count	%
Age	<40 years	13	13.0%
	41 to 50 years	33	33.0%
	51 to 60 years	31	31.0%
	>60 years	23	23.0%
	Total	100	100.0%

Majority of subjects were males (68%) and 32% were females. (Table 2)

Table 2: Gender distribution of subjects

		Count	%
Gender	Female	32	32.0%
	Male	68	68.0%
	Total	100	100.0%

Majority of subjects were diabetics and hypertensive from < 5 years duration (44% & 76.8% respectively). (Table 3)

Table 3: Duration of diabetes mellitus and hypertension

		Duration of DM		Duration of HTN	
		Count	%	Count	%
Duration of DM	<5 years	44	44.0%	63	76.8%
	6 to 10 years	31	31.0%	11	13.4%
	11 to 15 years	11	11.0%	4	4.9%
	>15 years	14	14.0%	4	4.9%

57% of subjects were on Oral hypoglycaemic agents (OHA) and 43% were on insulin in the study. (Table 4)

Table 4: Treatment taken by subjects in the study

		Count	%
Treatment	Insulin	43	43.0%
	OHA	57	57.0%
	Total	100	100.0%

On fundus examination 23% had proliferative diabetic retinopathy (PDR), 53% had Non proliferative diabetic retinopathy (NPDR) and 24% had no signs of DR.

Out of 53 subjects with NPDR, 19 had Mild, 28 had moderate and 6 subjects had severe NPDR. (Table 5)

Table 5: Fundus findings in the subjects

		Count	%
Fundus	PDR	23	23.0%
	Mild NPDR	19	19.0%
	Moderate NPDR	28	28.0%
	Severe NPDR	6	6.0%
	Normal	24	24.0%
	Total	100	100.0%

There was significant association between fundal changes and albumin excretion in urine. Among subjects with massive albuminuria, 64.7% of them had PDR. Similarly, among subjects with moderate albuminuria majority had moderate NPDR and subjects with microalbuminuria majority had normal fundus. This shows a strong association between fundal changes and albumin excretion. (Table 6)

No significant association was observed between haemoglobin levels and fundal changes. (Table 7)

Mean of total cholesterol (TC), High density lipoprotein (HDL), Low density lipoprotein (LDL) and Triglycerides (TG) was compared with the fundal changes. A significant difference was observed for total cholesterol and fundus changes, i.e., higher TC level was seen in PDR subjects than in NPDR. No difference was observed for TG, HDL and LDL levels. (Table 8)

Significant association was observed between total cholesterol and fundal changes. Majority of subjects with

Table 6: Association between fundus findings and albumin excretion

		Albumin Excretion					
		Micro albuminuria		Macro albuminuria		Massive Albuminuria	
		Count	%	Count	%	Count	%
Fundus	PDR	2	5.1%	10	22.7%	11	64.7%
	Mild NPDR	9	23.1%	9	20.5%	1	5.9%
	Moderate NPDR	10	25.6%	15	34.1%	3	17.6%
	Severe NPDR	2	5.1%	3	6.8%	1	5.9%
	Normal	16	41.0%	7	15.9%	1	5.9%
	Total	39	100.0%	44	100.0%	17	100.0%

χ 2 = 29.84, df = 8, p <0.001*

Table 7: Association between fundus changes and haemoglobin levels

		Hb			
		<12 gm/dl		>12 gm/dl	
		Count	%	Count	%
Fundus	PDR	22	25.3%	1	7.7%
	Mild NPDR	16	18.4%	3	23.1%
	Moderate NPDR	25	28.7%	3	23.1%
	Severe NPDR	6	6.9%	0	0.0%
	Normal	18	20.7%	6	46.2%
	Total	87	100.0%	13	100.0%

χ 2 = 5.735, df = 4, p = 0.220

Table 8: Association between fundus changes and lipid profile

		TC		HDL		LDL		TG	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Fundus	PDR	197.2	72.3	41.2	9.0	98.5	57.5	186.0	78.3
	Mild NPDR	167.0	58.2	46.0	23.2	76.1	28.3	165.6	71.2
	Moderate NPDR	164.8	45.5	47.1	20.1	76.4	28.6	157.5	70.1
	Severe NPDR	173.3	47.7	44.3	7.3	87.7	42.2	158.2	82.7
	Normal	134.6	39.8	51.5	19.0	82.5	32.8	182.0	93.5
	Total	165.9	57.4	46.4	18.1	83.6	39.0	171.5	78.4
P value		0.005*		0.420		0.278		0.674	

Table 9: Association between fundus changes and total cholesterol

		TC			
		<200		>200	
		Count	%	Count	%
Fundus	PDR	11	15.5%	12	41.4%
	Mild NPDR	14	19.7%	5	17.2%
	Moderate NPDR	20	28.2%	8	27.6%
	Severe NPDR	5	7.0%	1	3.4%
	Normal	21	29.6%	3	10.3%
	Total	71	100.0%	29	100.0%

TC >200 had PDR (41.4%). (Table 9)

No significant association was observed between HDL and Fundal changes. (Table 10)

Table 10: Association between fundus changes and HDL

		HDL			
		<40		>40	
		Count	%	Count	%
Fundus	PDR	12	32.4%	11	17.5%
	Mild NPDR	9	24.3%	10	15.9%
	Moderate NPDR	9	24.3%	19	30.2%
	Severe NPDR	1	2.7%	5	7.9%
	Normal	6	16.2%	18	28.6%
	Total	37	100.0%	63	100.0%

χ 2 = 5.978, df = 4, p = 0.201

No significant association was observed between LDL and Fundus changes. (Table 11)

Table 11: Association between fundus changes and LDL.

		LDL			
		<100		>100	
		Count	%	Count	%
Fundus	PDR	14	18.9%	9	34.6%
	Mild NPDR	14	18.9%	5	19.2%
	Moderate NPDR	21	28.4%	7	26.9%
	Severe NPDR	5	6.8%	1	3.8%
	Normal	20	27.0%	4	15.4%
	Total	74	100.0%	26	100.0%

No significant association was observed between TG and Fundus changes. (Table 12)

Table 12: Association between fundus changes and triglycerides

		TG			
		<150		>150	
		Count	%	Count	%
Fundus	PDR	9	20.0%	14	25.5%
	Mild NPDR	9	20.0%	10	18.2%
	Moderate NPDR	13	28.9%	15	27.3%
	Severe NPDR	4	8.9%	2	3.6%
	Normal	10	22.2%	14	25.5%
	Total	45	100.0%	55	100.0%

χ 2 = 1.632, df = 4, p = 0.803

No significant association was observed between Hb% and Albumin excretion. (Table 13)

There was no significant association between HbA1c and Albumin excretion. (Table 14)

There was no significant association between HbA1c and Diabetic Retinopathy. (Table 15)

4. Discussion

The microvascular complications of diabetes encompass long-term complications such as damage to the small blood vessels. These classically include retinopathy, nephropathy, and neuropathy. This may have devastating consequences, including blindness and end-stage renal disease. Some authors have identified associations between the complications themselves, and that one complication can serve as a risk factor for another. Recently, studies have shown that the presence of DR itself may increase the risk for diabetic nephropathy.

Retinopathy as a predictor of other diabetic complications, a study done by El Asrar AM[4] in the year 2001 concluded that retinopathy, especially the presence of PDR, is an independent predictor for nephropathy. The predictive value of retinopathy for nephropathy is stronger in patients with Insulin Dependent Diabetes Mellitus (IDDM) than in those with Non-Insulin Dependent Diabetes Mellitus (Non-IDDM). Therefore, it was suggested that ophthalmologists should refer patients with retinopathy for regular medical evaluations and vice-versa.

In another study conducted by Thivolet C et al[5] in 1990 concluded that, routine analysis of urinary albumin excretion rate in diabetics allows early detection of diabetic nephropathy and emphasizes the need for tight metabolic and blood pressure control.

A study conducted by Savage S, et al[6] in1996 concluded that increasing urine albumin excretion rate in Non-IDDM patients was associated with an increased prevalence of diabetic retinopathy, neuropathy, and cardiovascular disease. This suggests that urine albumin excretion rate may be more than an indicator of renal disease in these patients and, in fact, may reflect a state of generalized vascular damage occurring throughout the body.

In our study it was observed that there was significant association between fundus changes and albumin excretion in urine. Among subjects with massive albuminuria, 64.7% of them had PDR. Similarly, among subjects with moderate albuminuria majority had moderate NPDR and subjects with microalbuminuria majority had normal fundus. This shows a strong correlation between fundus changes and albumin excretion.

There was also a significant correlation between total cholesterol and fundal changes, i.e., higher TC was seen in PDR subjects than in NPDR. In our study, no difference was observed for TG, HDL and LDL levels. This is in contrast to a study by Alpana Mathur et al[7] in which it was found that triglyceride levels were significantly raised in subjects with DR as compared to those without DR showing a positive correlation. No such association was found between LDL and TC levels with the prevalence of diabetic retinopathy.

Table 13: Association between Albumin excretion and Haemoglobin %.

		Albumin Excretion					
		Microalbuminuria		Macroalbuminuria		Massive Albuminuria	
		Count	%	Count	%	Count	%
Hb	<12 gm/dl	33	84.6%	38	86.4%	16	94.1%
	>12 gm/dl	6	15.4%	6	13.6%	1	5.9%

χ 2 = 0.973, df = 2, p = 0.615

Table 14: Association between albumin excretion and HbA1c.

		Albumin Excretion					
		Micro albuminuria		Macro albuminuria		Massive Albuminuria	
		Count	%	Count	%	Count	%
HbA1c	<7	1	2.6%	3	6.8%	1	5.9%
	>7	38	97.4%	41	93.2%	16	94.1%
	Total	39	100.0%	44	100.0%	17	100.0%

χ 2 = 0.821, df = 2, p = 0.663

Table 15: Association between diabetic retinopathy and HbA1c

		HbA1cNew			
		<7		>7	
		Count	%	Count	%
Fundus	PDR	0	0.0%	23	24.2%
	Mild NPDR	2	40.0%	17	17.9%
	Moderate NPDR	2	40.0%	26	27.4%
	Severe NPDR	0	0.0%	6	6.3%
	Normal	1	20.0%	23	24.2%

5. Conclusion

Proliferative diabetic retinopathy is an independent predictor for nephropathy. Screening of all nephropathy patients can aid in the early diagnosis and management of diabetic retinopathy thereby preventing sight-threatening complications.

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Cite this article: Kalpana S, Sweekruthi G K, Anuradha A, Sharada M. Association between diabetic retinopathy and diabetic nephropathy: A clinical study. *Indian J Clin Exp Ophthalmol* 2022;8(1):137-141.