CORRELATION BETWEEN CLINICAL APPEARANCE OF RETINAL AND RENAL COMPLICATIONS OF DIABETES MELLITUS

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Introduction

Microangiopathy is the most specific long term complication of diabetes mellitus with major manifestations in retinal and glomerular vessels. Clinically retinopathy is diagnosed by ophthalmoscopy, and nephropathy by estimation of urinary protein. It is generally accepted that both retinopathy and nephropathy develop concurrently. Evidence of retinopathy is stated to be present in the vast majority of patients with diabetic nephropathy[1]. The purpose of the present communication is to report our findings on the incidence of retinopathy and nephropathy in all patients with diabetes mellitus at first admission to a special ward of the S.C.B. Medical College Hospital during a period of 7.5 years. These observations may be of special interest as all our patients have been carefully categorised to different clinical types such a I D D M, N I D D M and two varieties of malnutrition related diabetes mellitus (M R D M), protein deficient pancreatic diabetes (P D P D) and fibrocalculous pancreatic diabetes (F C P D).

Patients and Methods

637 patients admitted to the Diabetes (Endocrinology) Ward of the S.C.B. Medical College Hospital during a period of 7½ years (1977-85), are covered in the study. Each patient on admission was evaluated in detail regarding dietary history, nutritional status and biochemical profile besides clinical presentation. The patients were characterised as NIDDM, IDDM and MRDM depending on their socio-economic status, age of onset, proneness to ketosis, body mass index (BMI) and response to treatment. Specific note was taken of any complaint of visual disturbances or oedema. Ophthalmoscopy was performed in all cases. Routine examination of urine for the presence of protein was carried out by heat test. In all cases with positive result, protein content of 24 hours urine was estimated by sulphosalicylic acid method.

For the purpose of this report, retinopathy was diagnosed in the definite presence of microaneurysms or more advanced leisons. Nephropathy was considered to be present when the urinary protein was more than 0.5 gm/24 hr[2] in the absence of urinary tract infection or history of nephritis.

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Systemic blood pressure of 165/95 mm Hg or more, recorded on two or more occasions, was taken as hypertension. Renal insufficiency was diagnosed when the serum creatinine was over 2 mg per dl. Loss of visual acuity in the absence of cataract or any other obvious cause was attributed to retinopathy.

Observations

Distribution of clinical types of diabetes among the indoor patients studied is presented in Table 1. The mean age was below 20 years in case of IDDM, FCPD and PDPD (J-type) as against about 39 years for NIDDM. There was a male preponderance in all categories of diabetics. Information on family history, mean duration of diabetes, BMI and fasting blood glucose on admission is shown categorywise in the same table.

Table 1

Clinical types of diabetes among 637 indoor patients : Distribution and general information

Clinical type	Number	Mean age of onset in years	Sex distri-bution M : F	Mean BMI	FH	Duration of diabetes (years)	Mean FBG
NIDDM	450	38.6	3.4:1	M-20 F-18	+ve 40%	7.8	187.4
MRDM	152	19.3	2.6: 1	M-15 F-13.2	2%	8.9	232.2
PDPD	107						
FCPD	45	16.8	4:1	M-14.2 F-13	Nil	9.8	170.4
IDDM	35	14.3	3.8:1	F-12	6%	l2	116.1

BMI : Body Mass Index; FH : Family History; FBG : Fasting Blood Glucose

The incidence of retinopathy and nephropathy on clinical assessment is presented in Table 2. Retinopathy was commoner (21.4%) in the PDPD group as was nephropathy (10.2%) when compared to the other three groups of diabetics. Mean duration of known diabetes for isolated retinopathy or nephropathy was less (7.1 to 9.3 years) compared to patients suffering from both these complications (10.1 to 15.0 years) as shown in Table 3.

Table 2

Clinical incidence of retino-nephropathy among different categories of diabetes

Type of diabetes	Retinopathy No.	(%)	Nephropathy No.	(%)	Total either or both No.	(%)
NIDDM (n : 450)	35	(7.7)	38	(8.4)	57	(12.7)
PDPD (n : 107)	23	(21.4)	11	(10.2)	28	(26. 1)
FCPD (n : 45)	2	(4.4)	-		2	(4.4)
IDDM (n : 35)	2	(57)	2	(5.7)	2	(5.7)

Proteinuria - 0.5 gm/24 hours or more
Retinopathy - presence of microaneurysm or more advanced lesions.

Table 3

Mean duration of diabetes (years) and incidence of retino-nephropathy

	Retinopathy (alone)	Nephropathy (alone)	Both	None
NIDDM (n : 450)	8.82 ± 1.6	7.1 ± 0.5	12.3 ± 1.8	7.5 ± 2.6
PDPD (n : 107)	7.2 ± 0.4	9.3 ± 2.1	10.1 ± 0.8	10.2±1.7
FCPD (n : 45)	7.1± 0.3	-	-	9.07±0.6
IDDM (n : 35)	-	-	15.0 ± 2.1	9.0 ± 2.2

The severity of metabolic derangement as adjudged from the mean fasting blood glucose values (Table 4) was much higher in the PDPD group (232.2 ± 570 mg/dl) as compared to either NIDDM or FCPD. Microangiopathic complications were most common in this group of patients.

Out of 57 and 28 with both retinopathy and nephropathy in NIDDM and PDPD respectively, other complications were present only in 16 patients (Table 5).

Advanced retino-renal complications were absent in patients either with FCPD or PDPD (Table 6). Renal insufficiency was proportionately more frequent (5.7%) in IDDM than NIDDM (2.2%). Incidence of hypertension was near equal, but visual loss in the absence of cataract was found only among patients with NIDDM.

Table 4

Severity of diabetes and incidence of retino nephropathy

	Mean fasting blood glucose (mg/dl)			
	Retinopathy	Nephropathy	None	Total
NIDDM (n : 450)	193.2±63.5 (7.7)	205±52.24 (8.4)	164.1±36.5	187.4±21.0
PDPD (n : 107)	250.3±32.2 (21.4)	278±28.21 (10.2)	168.3±18.21	232.2±57.0
FCPD (n : 45)	192.2±22.6 (4.4)	-	148.6±12.8	170.4±30.8
IDDM (n : 35)	136.6±31.2 (5.7)	-	95.6±9.68	116.1±28.9

Figures in parenthesis indicate percentage of total.

Table 5

Concordance (C) and Discordance (D) in the incidence of Retinopathy and Nephropathy

Type of Diabetes	Retinopathy (alone)	Nephropathy (alone)	C	D	Total No.
NIDDM (n : 450)	19	22	16	41	57
PDPD (n : 107)	17	5	6	22	28
FCPD (n : 45)	2	--	--	2	2
IDDM (n : 35)	--	--	2	--	2

Table 6

Incidence of advanced retino-renal complications

Visual loss	Type of Diabetes	No.	Percentage
Visual loss (cataract)	NIDDM	9	(2)
Renal insufficiency	NIDDM	10	(2.2)
(Cr* > 2mg/dl)	IDDM	2	(5.7)
Hypertension	NIDDM	22	(4.8)
(B.P. > 165/95 mm)	IDDM	2	(5.7)

*Cr: Creatinine

Discussion

This report constitutes analysis of data from past case records. Yet as practically all the cases have been seen by one of the authors (K.C.S.) and the records have been kept on purpose; it may not bear all the stigmata of a retrospective study. It has been possible to examine each case carefully at admission into the hospital. The total number of patients analysed (637) is reasonably large. There is a satisfactory coverage of all the clinical types of diabetes encountered in this part of the country. In the natural course, the number of patients in categories FCPD and IDDM has been rather small for good comparison with the other types (Table 1).

For calculating duration of diabetes the date of detectionn had to be relied upon for want of better alternative. Severity of diabetes has been judged from levels of fasting blood glucose on admission. Estimation of HbA_1C was not available for half of the period covered and hence could not be utilised as a criterion.

Both retinopathy and nephropathy have been assessed by clinical methods, viz - ophthalmoscopy and estimation of 24 hours urinary protein. Venous dilatation alone has not been reckoned. Unequivocal presence of microaneurysms and more advanced lesions is taken as evidence of retinopathy in diabetics. It is generally agreed that persistent proteinuria of 0.5 gm or more in 24 hours (in the absence of haematuria or pyuria) is clinical indication of nephropathy in diabetics. Other forms of glomerulonephritis were excluded from history and available laboratory data. None of the 75 renal biopsies performed on diabetics during this period revealed any other form of glomerular disease.

Based on recent observations of Mogensen and coworkers[2] renal excretion of 50-200/ µgm of protein/mt is described as preclinical microalbuminuria and proteinuria above 300/µgm/mt (0.432 gm/day) is considered as the hallmark of clinical nephropathy, This is close to the generally accepted figure of 0.5g in 24 hours[3].

Mean age at onset in 450 unselected cases, of NIDDM (38.6 years) is lower than reported from the West. This has been noted by us and other workers in this country. Gross male predominance in all the types of diabetes is also a well known difference from the West[4]. As expected family history was positive much more often in cases with NIDDM than in the other types. Most diabetics were underweight. Mean BMI was within normal limit only in men with NIDDM. Patients of MRDM and IDDM were lean and grossly underweight. Mean duration in the different types of diabetes varied between 8 and 12 years at the first hospital attendance during the period of study. That they had to be admitted to the hospital indicates the presence of associated problems. Mean blood glucose was highest (232mg/dl) in cases with PDPD. It was lowest (116 mg/dl) in IDDM as they had to take insulin to avoid ketoacidosis (Table I).

Incidence of retinopathy in NIDDM (Table 2) appears to be lower in this series than is reported from the West while that of nephropathy is similar to observations made at Joslin Clinic[5]. Severe retinopathy is much less frequent among diabetics in India (New Delhi) compared to U.K. and Switzerland, while heavy proteinuria is commoner[6]. Reports on incidence of clinical microangiopathy in a sizeable series of patients with PDPD are unavailable to us. A high incidence of retinopathy (21.4%) among our patients is worthy of note as it may help in analysis of factors regulating the development of the complication. Both retinopathy and nephropathy were commoner among patients with PDPD with a total incidence of 26.1% compared to 12.7% in NIDDM and between 4 to 6% among the other two types.

There are many references in literature to correlate duration of diabetes with incidence of nephropathy as well as retinopathy[1]. These complications are notable by 10 years in IDDM, where onset is easily determined, and between 3 and 10 years in cases with NIDDM. Incidence rises steadily with duration upto 30 years and then levels off. In our study mean duration of diabetes in NIDDM was higher in patients with both complications (12.3 years) than with either or no complication. In patients with IDM the figures were 15 years and 9 years respectively (Table 3). Such relationship was not well marked in patients with PDPD or FCPD.

Much more striking was the correlation between severity of diabetes and incidence of microangiopathic complications. Not only were both retinopathy and nephropathy commoner in PDPD with higher levels of fasting blood glucose at admission than in other types, but mean blood glucose within each group was substantially higher in patients with either of the complications. (Table 4). The relationship between levels of hyperglycaemia and onset as well as progress of retinopathy has been fully documented by Western workers.

Clinically the "parallel natural course" followed by nephropathy and retinopathy has been clearly observed since the advent of insulin and prolongation of life. Generally, background retinopathy is already present by the time significant proteinuria indicates clinical nephropathy. Retinopathy is said to be present invariably in all patients with Keimmelstiel Wilson Syndrome. When our data in various clinical types of diabetes were analysed it was observed that the above dictum held true only for patients with IDDM, but not in cases of NIDDM or PDPD. Out of 57 patients of NIDDM with microangiopathic complications 16 had both, the remaining 4l had either retinopathy or nephropathy. The absence of retinopathy in 22 patients with clinical nephropathy was more surprising than absence of proteinuria in 19 patients with retinopathy. Among patients of PDPD, out of 28 cases with the complications, only 6 had both Five patients had proteinuria but no clinical evidence of retinopathy (Table 5). Although racial differences in incidence of nephropathy and advanced retinopathy have been documented by the recent WHO multinational study a wide divergence in the occurrence of retinopathy and nephropathy as seen in this study has scarcely been reported. On the other hand incidence of advanced retinal and renal disease was similar among patients with NIDDM (Table 6).

Thus our analysis of findings in 637 indoor patients of diabetes mellitus highlights, in addition to the distribution of clinical types in this part of the country, the facts that patients of PDPD, possibly because of greater hyperglycaemia, are more liable to develop both retinopathy and nephropathy and that among our patients with PDPD and NIDDM there remains a discordance between incidence of nephropathy and retinopathy. Observations on FCPD and IDDM cannot be generalised in view of small number of patients in these groups.

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