RENAL DISEASES IN DIABETES

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INTRODUCTION

Renal diseases in diabetes is an important cause of morbidity and mortality. At present three levels of albumin excretion rates are defined:-

i) 30 ug/min (normal)

ii) 30 – 200 (Micro-albuminuria)

iii) Persistently > 200 ug/min (Macro-albuminuria)

Thus presence of significant albuminuria confirmed on two consecutive intervals constitutes diabetes nephropathy [1]. Further evidence of increasing blood pressure and decrease in glomerular filtration rate characterizes complete syndrome.

PREVALENCE

Employing the above criteria, there are two studies from our country, one in 1975-78 conducted under the auspices of W.H.O., M.N.S.D. (14 countries), and second in 1986-89 conducted under aegis of I.C.M.R. (9 centres). The figure for diabetes renal disease from AIILMS, New Delhi were as follows.

Again the analysis of causes of mortality amongst diabetics in AIIMS Hospital, New Delhi over last three decades provide figures for renal and vascular disease as a cause of death from 22.7 to 40.2 per cent. (Table 1).

Table 1

Diabetes Renal Disease*

W.H.O.M.N.S.V.D. (1975-78) 14 Countries (Delhi Centre)				**I.C.M.R. (1986-89)** 9 Centres			
Duration (Yrs.)	0-6	7-13	≥=14		0-6	7-13	≥14
M (n=289)	9.3	10.7	23.0	M(n=262)	12.2	18.0	22.5
F (n=266)	4.2	5.7	13.6	F(n=245)	5.3	8.7	7.5

* Significant Albuminuria or Serum Creatinine > 1.5 mg/dl

Figures from other centres from our country are as follows. (Table 2).

Table 2

Mortality Data

AIIMS-Causes of Death (percent) amongst diabetics in the last 3 decades

Cause of Death	**1966**	**1976**	**1986**
	n=75	n=560	n=580
DKA	9.3	12.4	6.5
Total Vascular Disease	76.0	69.0	74.5
Cardiac	42		
Cereberal	11.0	11.7	10.5
Renal	22.7	28.2	40.2
Cirrhosis	6.7	3.2	3.3
Infections	2.7	5.5	9.2
Others	4.0	9.9	6.5

Lily John from CMC Vellore[2] reported macroalbuminuria in 8.9% of NIDDs and micro albuminuria in 19.7 per cent of NIDDs.

Chugh from PGI Chandigarh[3] found that out of 407 patients of ESRD, 26% were due to diabetes nephropathy.

Amongst Asian Indian in U.K. , diabetic nephropathy is observed in 28.6 percent [4] and 22.3 per cent[5] and cause for this high figure is stated ethnic predisposition. Genetic factors have been implicated in the susceptibility of individuals to proteinuria.

ASSOCIATED RISK FACTORS

A further analysis of data from the two studies as to correlated factors brings out the following significant features.

BMI is negatively correlated e.g. lean persons are amore prone to develop diabetes renal disease.

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In WHO study, duration of diabetes, systolic blood pressure and serum cholesterol had significant relationship, while in the ICMR study, systolic blood pressure and degree of glyucaemic control showed this relationship.

Most of the above data referred related to NIDDM as these studies included diabetic population between 25-65 years of age.

VARIATION IN RELATION TO TYPE OF DIABETES

It is important to note that certain subtle differences of diabetes renal disease are observable depending on the clinical characteristics of diabetes: Type 1 (IDDM), or Type 2 (NIDDM). (Table3).

Table 3
Differences between IDDM and NIDDM Regarding Diabetes Renal Disease

Feature	IDDM	NIDDM
Microproteinuria Presages diabetes nephropathy	80%	25%
Hypertension present Prior to proteinuria	No	20-30%
Characteristic of hypertension	Systemic	Isolated systolic
Duration related	Yes	--

STRUCTURE FUNCTION RELATIONSHIP

When an attempt is made for an in depth study histological features of renal disease amongst diabetics, it is to be borne in mind that in approximately one fourth instances, there may be presence of non-interstitial disease, minimal lesion nephropathy, or mesangio-proliferative nephropathy. Followings studies elaborate this aspect of diabetes renal disease.

MANAGEMENT ASPECTS

Followings modalities of treatment are considered relevant at the present time:

i. Intensive insulin therapy for metabolic control

ii. Use of ACE inhibitors

iii. Low protein diets.

i) The DCCT trial, which involved 1441-IDDM patients who were a) either given intensive therapy (3-4 insulin injection/day and four blood glucose estimations per day with adjustment of daily insulin dose) or (b) given conventional therapy (1-2 insulin injections and no adjustment of blood glucose on daily basis).

There was a mean follow-up period of 6-5 years. In the intensive group mean blood glucose achieved was 155 ± 30 mg/dl while in intensive group mean blood glucose value was 231 ± 55 mg/dl Albuminuria (> 300 mg/24 hrs) was refused by 54 per cent (95% Cl, 19-74 per cent).

ii) In a meta-regression analysis of effect of antihypertensive therapy on kidneys in patients with diabetes, kasiskse et al[6] observed that the mean reduction in urinary protein excretion was greater in patients treated with ACE inhibitors than those treated with other anti-hypertensive agents or with placebo.

The effect was due to changes either in the size or charge selective properties of the glomerular capillary wall or reduction in glomerular capillary hydraulic pressure. This effect seem to be forthcoming even amongst those with diabetes tenal disease but no hypertension, and relates to alterations in the intrinsic properties of the glomerular barrier i.e. renoportective effect[7].

iii) Low protein diets (0.6 g/kg body weight). This has shown beneficial effects in instances with dicompensated renal function. The possible mechanism seems to be a reduction in hyperfiltration or reduction in certain hormonal levels, e.g. glucagons, prostaglandin or atrial natriuretic peptide or a decrease in phosphate load.

The issues on comparison of source of proteins, animal versus vegetable or in regard to adjustment of protein intake related to maintenance of nitrogen balance and pre-determination of ‘responder’ verses ‘non-responder’ eludes definite answer at present and requires further investigations.

ATYPICAL CLINICAL PRESENTATIONS

Two interesting clinical presentations in regard to diabetes renal disease are worth mentioning. One is presentation in cases with diabetic nephropathy and hypertension receiving treatment with diuretics for prolonged periods. Patients complaint of extreme weakness and irregular heart beats. There is hyperkalemia, acidosis, serum sodium is normal or low and blood glucose raised. Plasma rennin value is low and non-responsive to stimulation with angiotensin.

The clinical state is ascribed to hyporeninaemia with hypoaldosteronism. The relief is through administration of (flourdocortisone) (Florinef) 0.1-0.2 mg/day. Patients on this regime make very good recovery. (Table 4).

Table 4
Prevalence of renal disease unrelated to diabetes [8]

	Year	No. of diabetics	Percent with non-diabetic nephropathy	Reference
India	1968	36	27%	[8]
Abroad	1990	136	28%	[9]
	1990	33	33%	[7]
	1991	35	28.6%	[10]

The other observation has been a state of "insulin resistance" in diabetics following renal transplant. Partly one may ascribe this to corticosteroids or alteration in the immunological profile. There seems no mention of such clinical presentation so far in the literature.

One has been able to deal with this situation only by restoring to continuous insulin administration by insulin pump. However there is no longer any apprehension for advise that for end stage renal failure transplant from a live related donor offers the best chance of rehabilitation and improved quality of life.

CONCLUSIONS

1. Prevalence of diabetes renal disease is quite significant in our population.

2. It is now being increasingly recognized that macroalbuminuria may as well be a predictor of cardio-vascular disease in diabetics. However significance of macroalbuminuria relates to the type of diabetes. Again in one third instances of macroalbuminuria, the cause may be a renal disease unrelated to diabetes.

3. Attention is drawn to some of the management issues i. e. intensive insulin therapy for hyperglycemia, use of ACE inhibitors for hypertension and institution of low protein diet regimes that are effective in slowing the rate of progression of diabetes renal disease.

4. Again with end stage renal disease (GFR < 15 ml/min) resource to transplantation can salvage the situation and restore good functional life.

5. Though such reparative or reconstructive measures offer a new lease of life, still commendable will be effective primary and secondary preventive measures by improving health, education and diabetes management strategies.

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