Clinical diabetic nephropathy in a tropical African population

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Summary

Diabetic nephropathy is the single most important disorder leading to renal failure in adults in the Western countries and it is among the first three major causes of end stage renal disease in Nigeria. The aim of this study is to show the features of clinical diabetic nephropathy in the Olabisi Onabanjo University Teaching Hospital, Ogun State, Nigeria. The study group consists of 342 consecutive diabetic patients with persistent proteinuria (positive albustix) and diabetic retinopathy, seen from January 2000 to June 2001 in the Ogun State University Teaching Hospital, Sagamu. Clinical and laboratory parameters were recorded. Students' t-test and Spearman correlation coefficient were used in analysis. The frequency of occurrence of clinical diabetic nephropathy is 28.4% with majority already symptomatic despite normal biochemistry. Mean ages of type 1 and type 2 are 26±7.9 years and 53.4± 6.3 years respectively with a sex ratio of 1.2:1. Mean duration of disease is 6.5± 3.6 years and 9.4±4.1 years respectively. Two hundred and seventy-one (79.2%) patients were hypertensive. Nephrotic syndrome is not a common presentation. Diabetic nephropathy is a significant problem in this environment.

Keywords: ***Diabetes nephropathy, Clinical review, Nigeria.***

Résumé

La néphropathie diabétique est un trouble le plus considérable aboutissant à l'insuffisance rénale chez des adultes aux pays de l'ouest/occidental et elle est parmi les trois premier causes majeur de la maladie rénale au denier étape au Nigeria.

L'objet de cet étude est de mettre en relief les traits de la néphropathie diabétique clinique au centre hospitalo-universitaire d'Olabisi Onabanjo, état d'Ogun au Nigeria. Le groupe d'étude consiste de 342 patients diabétiques consécutive atteints de la proteinurie incessante (albustix positif) et rétinopathie diabétique, vu de janvier 2000 au juin 2001, au centre hospitalo-universitaire d'état d'Ogun, Sagamu.

Des paramètres laboratoires et cliniques ont été notés. Etudiants T-Test et coefficient Spearman corrélation ont été utilisés dans l'analyse. La fréquence de l'incidence de la néphropathie diabétique clinique est 28,4% avec le grand nombre déjà symptomatique en dépit de la biochimie normale. Ages moyen de type 1 et type 2 sont 26,3±7,9 ans et 53,4 ± 6,3 ans respectivement dans une proportion du sexe de 1,2:1. La durée moyenne de la maladie est 6,5 ± 3,6 ans et 9,4 ± 4,1 ans respectivement.

Deux cent soixante onze soit 79,2% des patients étaient hypertensives. Syndrome néphrétique n'est pas fréquent au cours de la présentation. La néphropathie diabétique est un problème important dans ce milieu.

Introduction

Diabetes mellitus refers to a metabolic disorder, characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects insulin secretion, insulin action, or both[1,2]. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs including the kidneys. Type 1 diabetes mellitus encompasses the majority of diabetics, which are primarily due to pancreatic islet beta-cell destruction and are prone to ketoacidosis[1,2]. They include those cases attributable to an autoimmune process, as well as those with beta-cell destruction and who are prone to ketoacidosis for which neither an aetiology nor a pathogenesis is known (idiopathic). It does not include those forms of beta-cell destruction or failure to which specific causes can be assigned (e.g. cystic fibrosis, mitochondrial defects, etc.)[1,2]. Type 2 diabetes mellitus however, is the major form of diabetes and is characterised by disorders of insulin action and insulin secretion, either, of which may be the predominant feature[2]. It is usually associated with insulin resistance. The national prevalence of diabetes mellitus in Nigeria is 2.2%[3].

Chronic glomerulonephritis, hypertension, diabetes mellitus and obstructive uropathy[4] are the most common causes of chronic renal disease among Nigerians. In the Western countries and Japan, diabetic nephropathy is the single most important disorder leading to renal failure in adults accounting for more than 25% of all end stage renal disease[5]. In Nigeria there is a progressive rise in the incidence of diabetic nephropathy from 19% in 1971[6] to 42.5% in 1988[7]. Table 1 shows a comprehensive scheme of stages in diabetic nephropathy. Diagnosis of clinical diabetic nephropathy is defined by the presence of persistently positive urinary dipstick test for albumin in a person with diabetes (or a urinary albumin excretion rate > 0.3g per day) in the absence of other renal disease[8,9,10]. It is frequently accompanied or followed by the presence of hypertension and deteriorating kidney function[9]. Retinopathy is almost always present and the risks for coronary heart disease and mortality are much higher than in patients who do not have albuminuria[9,10,11]. The prevalence of clinical nephropathy has been reported to be between 15% and 40% generally[9,10,11] in the developed countries. The aim of this study is to show the features of clinical diabetic nephropathy in the Ogun State University Teaching Hospital, Nigeria.

Methodology

The study group consists of 342 consecutive diabetic patients with persistent proteinuria (positive albustix), seen from January 2000 to June 2001, in the Ogun State University Teaching Hospital, Sagamu. The inclusion criteria were prior clinical diagnosis of diabetes mellitus and medical treatment (either insulin therapy (type 1) or oral hypoglycaemic agent (type 2) and/or dietary management) for at least five years duration, presence of diabetic retinopathy, no clinical or laboratory evidence of any other kidney disease or renal tract disease and the presence of persistent proteinuria. Persistent proteinuria is defined as dipstick proteinuria on early morning urine samples at least on 3 occasions each visit at least 4 weeks apart. The exclusion

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criteria include diabetes mellitus of less than five years duration, urinary tract infection and infestation, congestive cardiac failure, pregnancy, history suggestive of chronic glomerulonephritis and absence of diabetic retinopathy. The subjects were divided into type 1 and type 2 diabetics. Type 1 patients are those on insulin therapy while type 2 patients are those diabetics on oral hypoglycaemic agents. Patients whose diabetes has been controlled on diet but previously on insulin control or oral hypoglycaemic agents were classified as type 1 and type 2 respectively.

Clinical parameters including current age, age of onset, sex and duration of diabetes mellitus, drug therapy, clinical symptoms and blood pressure were recorded. Blood pressure was measured twice during the study while trying to establish persistent proteinuria and was recorded to the nearest 2mmHg. Cuff size 20–31cm was used in patients with an upper arm circumference above 32cm. Blood pressure was measured twice during the study while trying to establish persistent proteinuria and recorded to the nearest 2mmHg. Systolic and diastolic blood pressures were taken as the appearance and disappearance of the Korotkoff sounds (phases I & V respectively). Hypertension was defined as systolic blood pressures of $\geq$ 140mmHg and diastolic blood pressure of >90mmHg (taken on at least two different occasions). Patients already on antihypertensives were taken as hypertensive. Laboratory parameters to assess renal function, serum proteins, cholesterol, triglycerides, fasting and 2 hours postprandial blood sugars (on two occasions), and the packed cell volume were estimated. Urinalysis and urine microscopy, 24-hours urinary protein and creatinine clearance were done. Completeness of 24-hours urine collections was assessed by direct questioning and urinary creatinine.

Quantitative data was expressed as mean ±S.D. Student's t-test was used to assess the difference between the various subject groups. Correlation was by Spearman correlation coefficient and significance was taken at $p<0.05$.

Results

One thousand, two hundred and five diabetics were seen during the study period out of which three hundred and forty two fulfilled the inclusion criteria. The frequency of occurrence of clinical diabetic nephropathy among the diabetics studied is thus 28.4%, eight (2.3%) been type 1 and three hundred and thirty four (97.7%) been type 2.

The patients include 184 males and 158 females with a male to female ratio of 1.2:1. The ages of the patients ranged between 16 – 78 years with a mean age of 49.4 ± 2.8 years. The peak age incidence was in the fourth decade with mean ages being 26.3 ± 7.9 years and 53.4± 6.3 years for type 1 and type 2 respectively ($p<0.05$). The age at onset of disease ranged from 10 to 63 years with a mean of 40.1 ± 10.3 years; while the mean age at onset of disease in type 1 and type 2 are 12.3 ± 2.7 years and 44.9±9.6 years ($p<0.01$) respectively. The duration of disease was 6.5 ± 3.6 years for type 1 and 9.4 ± 4.1 years for type 2 diabetics.

Thirty-five patients (10.2%) had protracted lethargy and appetite was impaired in 25 (7.3%) of the patients. Thirteen (3.9%) out of the type 2 populations had uraemic symptoms (nausea, vomiting and hiccoughs). Two hundred and seventy one patients (79.2%) had a history of systemic hypertension of varying severity and were on treatment. Six out of eight (75%) of type 1 patients had associated hypertension and were re-

Table 1 Comprehensive scheme of stages in diabetic nephropathy

Stage	Onset	UAE	GFR* Ml/Min	Other functional abnormality	Structural abnormalities	% progression to next stage
Stage 1 Renal Hypertrophy and Hyperfunction	Present at time of of diagnosis of diabetes mellitus	May be increased	–	Large kidney	Glomerular hypertrophy normal basement membrane normal fractional mesangial volume	100%
Stage 2 Silent Phase	By 2-3 years after diagnosis of diabetes mellitus	Normal (may be increased during stress)	–	–	Increasing basement membane thickness and mesangial expansion	35 – 40%
Stage 3 Incipient Diabetic Nephropathy	7 – 15 years after diagnosis of diabetes mellitus	20 – 200 microgram/min	– – – –	–	Severity between stages 2 and 4 increasing glomerulosclerosis	80 – 100%
Stage 4 Overt Diabetic Nephropathy	10 – 30 years after diagnosis of diabetes mellitus	—	Normal or	Clinical proteinuria UAE > 200 microgram/min	Widespread glomerulosclerosis	75 – 100%
Stage 5 End stage Renal failure	20 – 40 years after diagnosis of diabetes mellitus	Decreasing	<10ml/min	ESRD	Generalised glomerulosclerosis	

**GFR – Glomerular filtration rate*
+UAE – Urinary albumin excretion rate

Table 2 Mean biochemical values of the 342 diabetics studied

Electrolytes	Mean values
Sodium	131.7 ± 0.6 mmol/l
Chloride	103.1 ± 0.6 mmol/l
Potassium	3.6 ± 0.1 mmol/l
Bicarbonate	25.5 ± 0.4 mmol/l
Creatinine	82.4 ± 8.8 Umol/l
Creatinine clearance	0.74 ± 03 ml/s
Urea	6.6 ± 0.8 mmol/
Cholesterol	3.7 ± 0.9 mmol/l
Triglyceride mmol/l	1.24 ± 0.03
Fasting blood sugar	6.7 ± 0.6 mmol/l
2 hour post prandial blood sugar	10.5 ± 0.6 mmol/

ceiving treatment. Out of the type 2 diabetics, one hundred and twenty seven (38.0%) patients had mild hypertension, 74 (22.2%) patients had moderate hypertension while 37(11.1%) had severe hypertension. Seventy-seven (22.5%) patients had systolic blood pressure between 140mmHg-160mmHg and 21(6.1%) had systolic blood pressure > 161mmHg.

The mean values of serum electrolytes were within normal limits (Table 2). The mean value of serum urea is 6.6±0.14mmol/l (range = 2.5 – 45.3mmol/1). Three hundred and eight (90.1%) patients had serum urea value less than 8.3mmol/1. Two hundred and ninety-one (85.1%) out of the three hundred and forty-two patients had serum creatinine less than 141.41 Umol/1 while 41(11.9%), 7(2.0%) and 3(0.9%) had serum creatinine between 141.4 – 176.8 Umol/11, 185.6 – 265.2 Umol/1 and >274 Umol/1 respectively. The range of values of creatinine clearance is 0.17ml/s – 1.36ml/s with a mean value of 0.75 – 0.03ml/s ± 1.9mls per min. There were no patients with hyperfiltration. There is negative correlation between the degree of proteinuria and creatinine clearance ($r = -3307$ $p<0.05$). No significant relationship/correlation was demonstrated between creatinine clearance and control of blood sugar, type of diabetes mellitus duration of disease and presence of hypertension. There was no significant correlation between the duration of diabetes and the development of diabetic nephropathy ($r = 0.1835$ $p> 0.05$).

Discussion

Previous studies of clinical diabetic nephropathy in the same environment gave figures ranging from 19% in 1971[6] to 42.5% in 1988[7]. The figure of 28.4% obtained in the present study, although suggesting a fall in the frequency of occurrence of clinical diabetic nephropathy in the study population, should be interpreted with caution. The entry criteria used in this study excluded patients that were erroneously included in earlier studies e.g patients with intermittent proteinuria. The presence of diabetic retinopathy also excluded some patients without clinical diabetic nephropathy that otherwise would have been included since retinopathy is almost always present in clinical diabetic nephropathy[9,10,11]. Abdullah[12] documented a figure of 46% in Kenya. Lower figures were however recorded in Sudan (11.6%)13 and Ethiopia (6%)[14].

It has been observed that type 2 diabetes mellitus accounts for approximately 75% of cases of end stage renal disease due to diabetic nephropathy because the population of patients with type 2 is at least ten times larger than the population with type 2[11] in the Western countries. Only 8 patients (2.3%) had type 1 diabetes out of the 342 diabetics studied. Possible reasons are that type 1 patients are more likely to die out in this environment due to the exhorbitant costs of both insulin therapy and the management of the acute metabolic complications. The high prevalence of infections, which acutely increase their insulin requirements, is another factor of financial importance[15].

The likely role played by the male sex hormones in diabetic nephropathy has been stressed[11]. There is a male preponderance with a male to female ratio of 1.2:1 in this study ($p<0.05$). There was a statistically significant difference in the mean ages of the patients (type 1 vs type 2) both at contact with the study and at onset of diabetes. Taking into consideration the age at diagnosis, all the type 1 patients were diagnosed below 40 years of age and type 2 after 40 years of age.

The mean duration of disease of 6.5 ± 3.6 years for type 1 and 9.4 ± 4.1 years for type 2 diabetics is higher than previous studies in the same environment[16,17]. The increased mean duration of disease recorded may be due to increase longevity, awareness and better management of diabetic state when compared to the situation in the early sixties (Thomas[16] recorded a mean of 3.9 years and Greenwood and Taylor[17], a mean of 4.2 years among the same tribe).

Previous workers[17,18,19] have observed that diabetics tolerate uraemia less well than patients with other types of kidney disease. Some of the patients in this study were already symptomatic despite the normal creatinine and urea values at the time of the study. The occurrence of hypertension in about 75% of type 1 diabetics should arouse the suspicion of diabetic nephropathy in young type 1 patients who develop elevated blood pressure. The classical nephrotic syndrome occurs in 5 – 10% of cases of diabetic nephropathy[20]. This however is not common amongst the patients studied and it may be difficult to explain.

In conclusion, clinical diabetic nephropathy is a significant problem in this environment.

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