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Diseases causing chronic renal failure in Nigerians — a prospective study of 100 cases

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Summary

There are indications that there is an increased risk of chronic renal failure (CRF) in the Negroid race, yet few studies have been carried out in the native 'black' environment. A clinicopathological study of 100 consecutive Nigerian subjects with CRF, seen over a 3-year period, is presented. Primary chronic glomerulonephritis (CGN) accounted for 50, accelerated hypertension for 25, and various aetiological entities for a further nine; these included, chronic pyelonephritis (two), diabetic nephropathy (two), calculous nephropathy (one), toxaemia of pregnancy (one), renal dysplasia (one), tuberculosis (one) and polycystic disease in the ninth subject. In 16 cases, no definitive aetiological diagnosis could be made. Combinations of the following features, protracted hypertension, proteinuria, significant analgesic intake and gouty arthritis, were observed. CGN and accelerated hypertension still remain the leading causes of CRF, while diseases such as diabetes mellitus and chronic pyelonephritis do not contribute significantly to CRF in Nigerians. Recognition of the early features and the causes of CRF would considerably reduce the prevalence of this condition.

Résumé

Nos observations montrent qu'il y a des risques croissants de la faillité rénale chronique (FRC) parmi les gens de la race noire pourtant peu d'études ont été effectués parmi les Noirs du continent noir. Une étude clinicopathologique de 100 malades consécutifs venant de Nigéria et ayant la crise rénale chronique ont été examinés pendant trois ans. Cinquante d'entre eux avaient glomérulonéphritis chronique primaire (GCP), 25 avaient l'hypertension accélérée et neuf avaient diverses entités étiologiques. Ces dernières comprennaient deux de la pyélonéphritis chronique, deux de la néphropathie diabétique, un de la néphropathie calculeuse, un de la toxémie gravidique, un de la dysplasie rénale, un de la tuberculose et un d'une maladie polycystique. Dans 16 des cas, aucune diagnose étiologique pourrait être effectuée. Une combinaison des caractéristiques suivantes i.e. hypertension prolongée, protéinurie, une dose analgésique importante, arthrite goutteuse, ont été observées en eux. Hypertension accélérée et glomérulonéphritis chronique primaire restent les causes de la FRC les plus notables, tandis que les maladies comme le diabète mellitus et la pyélonéphritis ne contribuent pas principalement à la FRC parmi les Nigérians. Identification des caractéristiques précoces de la FRC et les facteurs causatifs réduiront considérablement la prévalence de cette condition.

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Introduction

Chronic renal failure (CRF) poses serious economic and epidemiological problems with regard to the enormous costs of management and the multiplicity of causes, which vary from one population to the other. Balkan nephropathy accounts for a significant proportion of cases of CRF in the Balkan countries [1], while amyloidosis resulting from familial Mediterranean fever is very prevalent in Israel [2]. Similarly, analgesic nephropathy contributes

significantly to the causes of CRF in Sweden [3]. Chronic glomerulonephritis and hypertension also account for a staggering proportion of CRF in studies from the tropics [4–9].

Even though most of the available studies were hospital-based, there are indications of an increased risk of CRF in the Negroid populations [4,5,10]. The majority of these populations live in developing countries which cannot bear the financial burden of management of end stage renal disease (ESRD). It is therefore mandatory that efforts should be geared towards (a) determining the causes of CRF with a view to planning preventive measures for those who are amenable, and (b) identifying its early or protean manifestations when progression of the disease could be influenced by a relatively cheaper therapeutic regimen [11].

Very limited studies have been carried out to highlight these aspects of CRF in Nigerians [7,8]. In an attempt to define further the pattern of causes of CRF, and determine its protean manifestations, we have carried out a clinicopathological study of 100 cases, seen over a 3-year period, on the medical wards of the Ife State Hospital and the Seventh Day Adventist Hospital, Ile-Ife. In one-third of the cases we obtained renal histopathological features either by percutaneous renal biopsy or at autopsy.

Subjects and methods

Between January 1983 and December 1985, all consecutive patients with serum creatinine values consistently above 2 mg/100 ml, and presenting with early features of CRF such as nocturia, lassitude or nausea, were studied.

Their medical history was obtained with a protocol designed to highlight diagnostic features of more readily recognizable disease entities causing CRF, (a) primary glomerulonephritis (CGN), (b) accelerated hypertension and (c) chronic pyelonephritis. Clinical features which are suggestive of other causes of CRF, such as diabetes melllitus, polycystic disease, analgesic nephropathy and systemic lupus erythematosus, were also sought.

The definitive criteria for diagnosis of primary CGN include: (a) verified history and biochemical evidence of the nephrotic syndrome at least 6 months before presentation, (b) past medical history of profuse proteinuria detected either biochemically or recognized by the subject as frothy urine, and (c) recurrent history of pre-eclamptic toxaemia in pregnancies.

Persistent accelerated hypertension is diagnosed in the presence of a combination of the following features: history of recurrent and intense throbbing headaches requiring repeated analgesic consumption, usually associated with blurring of vision, for at least 1 year; a diastolic blood pressure usually above 130 mmHg; the presence of advanced retinopathy including haemorrhage and exudates, with or without papilloedema; the presence of clinical features of left ventricular hypertrophy and aortic unfolding; the presence of microscopic haematuria and usually only moderate proteinuria; and the lack of a past medical history of the nephrotic syndrome.

The relevant clinical features for the diagnosis of chronic pyelonephritis include episodes of urinary tract infection, diagnosed by the classical clinical features with or without laboratory evidence. At least three episodes per year for at least 2 years were considered to be significant. This was supported by the presence of polymorphs during urine microscopy, and repeatedly positive urine cultures on follow-up. Subjects strongly suspected to have chronic pyelonephritis also had a high dose intravenous urogram (IVU) performed to delineate renal outline.

Other miscellaneous causes, e.g. diabetes mellitus, polycystic kidney disease, etc. did not pose any clinical diagnostic problem, and a number of them already had histological diagnosis from either renal biopsy or autopsy. Subjects in whom a definitive aetiological factor could not be implicated, because of either (a) a lack of relevant history, or (b) the presence of multiple factors and, when available, ill-defined renal histology, were designated as 'unclassified'.

Histological diagnostic criteria

Primary CGN was diagnosed by renal biopsy in cases with nephrotic syndrome, 1–2 years before CRF complicated the disease. In cases after autopsy, histological diagnosis rested on the following findings: finely granular and symmetrically shrunken kidneys; reduced corti-

cal thickness, normal medulla, pelvis and ureters; predominant glomerular involvement with no or few hypertensive vascular changes; and the presence of diffuse hyalinization associated with proliferative changes in residual glomeruli.

Accelerated hypertension was diagnosed on the basis of gross vascular changes, with end-arteritis, onion skinning, re-duplication of internal elastic lamina, cellular proliferation of intima which may have undergone fibrosis, and the presence or lack of fibrinoid necrosis. There is usually glomerular hyalinization and shrinkage leaving a patent urinary space.

Results

In the 3-year period, 1242 subjects comprising 700 males and 542 females were admitted. Of these, 100 presented with CRF. These comprised 64 males and 36 females with ages ranging from 12 to 61 years, mean 33.4 ± 12.9 years (Fig. 1). The mean serum creatinine level was 13.2 ± 9.6 mg/100 ml (range 2.3–36.8).

Four categories of clinical diagnosis were made. In 33 subjects these were corroborated by histology, obtained either by renal biopsy or autopsy (Table 1). Using our criteria, 50 of the subjects had primary CGN. The diagnosis was confirmed histologically in 19 of these. In five others it was confirmed at autopsy. Twenty-five subjects had accelerated hypertension, with diagnosis confirmed by autopsy in five.

In nine subjects various causes were responsible for the CRF (Table 2). In six of these, the clinical diagnosis was corroborated by histology. The renal histological features of toxaemia of pregnancy were obtained in one case and chronic pyelonephritis was clinically diagnosed in two grand multiparous women. This diagnosis was confirmed by IVU in one, but only strongly suspected on clinical grounds in the other. Two subjects had diabetic nephropathy; in one of them the characteristic Kimmelstiel–Wilson nodules and glomerulosclerosis were found on renal histology. Calculous nephropathy with pyelonephritis was observed in one case, and this was confirmed at autopsy.

Autopsy findings of polycystic kidney disease were found in one 55-year-old man, while renal dysplasia was reported in a 14-year-old schoolboy. Tuberculous adenitis coexisted with CRF in one subject, the kidneys could not be opacified on IVU, but the delayed progression of CRF with anti-tuberculous therapy made renal tuberculosis a distinct possibility.

The aetiology of the renal disease could not be classified in 16 subjects, 10 males and six

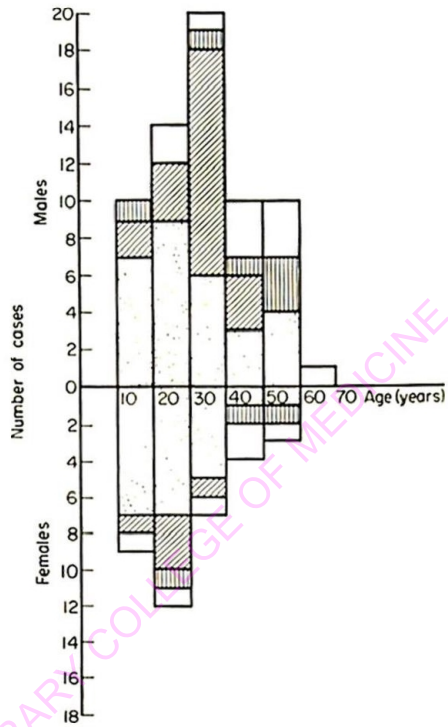

Fig. 1. Histogram of age-sex distribution with respect to diagnosis. (□) 'unclassified'; (▥) miscellaneous; (▨) accelerated hypertension; (▩) CGN.

Table 1. Pattern of disease and method of diagnosis

	Method of diagnosis			
Disease group	Clinical	Biopsy	Autopsy	Total
CGN	31	11	8	50
Accelerated hypertension	20	—	5	25
Miscellaneous	3	2	4	9
'Unclassified'	16	—	4	16

Table 2. Miscellaneous group — pattern of disease

Type of disease	No. of subjects	Method of diagnosis	
		Clinical	Histological
Severe toxaemia of pregnancy	1		1
Chronic pyelonephritis	2	2	
Diabetes mellitus	2	1	1
Calculous nephropathy	1		1
Polycystic renal disease	1		1
Renal dysplasia	1		1
TB adenitis + renal failure	1		1

females (Table 3). In four of these, autopsy revealed global glomerulosclerosis and florid hypertensive changes. Renal angiography in two others revealed bilateral shrunken kidneys with regular renal outlines which excluded a diagnosis of chronic pyelonephritis. All of them had features of protracted hypertension such as aortic unfolding and cardiomegaly. The diastolic blood pressure ranged between 100 mmHg and 150 mmHg (mean 120 ± 15.1 mmHg). Advanced retinopathy of grades 3–4 was observed in five subjects. Proteinuria was gross (>300 mg/100 ml) in five, and moderate (<300 mg/100 ml) in eight subjects. Three of the subjects had taken a variety of analgesics in an apparently significant quantity for at least 6 months, but they had not experienced macroscopic haematuria. Two subjects had coexisting gouty arthritis.

The mean ages of the clinical groups of subjects were as follows: primary CGN 29.9 ± 12.9; accelerated hypertension 33.1 ± 4.1; miscellaneous 43.5 ± 13.5, with the 'unclassified' group being 42.3 ± 12.3 years. The apparent difference between the means of ages of the groups of primary CGN and accelerated hypertension was not statistically significant.

The sex distribution of the subjects in the

Table 3. Clinical features of the 'unclassified' group

Parameter	Pattern
Number and sex distribution	16; 10 male, 6 female
Age: range; mean (years)	18–61; 42.3 ± 12.3
History of body swelling	Present in 6
Evidence of protracted hypertension	Present in all
Hypertensive disease in pregnancy	3 out of 6 females
Significant analgesic intake	3
Diastolic blood pressure: range; mean (mmHg)	100–150; 120 ± 15.1
*Proteinuria	
Moderate (<300 mg/100 ml)	8
Gross (≥300 mg/100 ml)	5
*Retinopathy	
Normal	2
Grade I–II	3
Grade III–IV	5
Serum creatinine: range; mean (mg/100 ml)	2.4–36.8; 14.4 ± 11.2
Coexisting disease — gout	2

*Investigation could not be carried out in all subjects.

respective clinical classes is demonstrated in Fig. 1. There was a high proportion of the males (20 out of 25) in the group with accelerated hypertension than in the group with primary CGN. This contrasted sharply with the male: female sex ratio of 1.2:1 for total admissions during the period of study.

The 'clinical onset of illness' was rather short in 39 subjects, being less than 3 months, but a probe into the history revealed a disproportionately long period of significant nocturia (at least twice per night) in 52 subjects.

We observed that a history of throbbing headaches, troublesome enough to require analgesic ingestion, was prevalent amongst the subjects. While this was present in 20 (80%) of the subjects with accelerated hypertension, it was observed in only 24 (48%) of the subjects with primary CGN. The mean diastolic blood pressure was 115.8 ± 27.3 mmHg in subjects with CGN; 143.4 ± 13.6 mmHg in accelerated hypertension; 120 ± 15.1 mmHg in the unclassified group, while it was 106.6 ± 13.3 mmHg in the miscellaneous group (Table 4). There was a statistically significant ($P < 0.01$) difference between the means of the diastolic blood pressure of the subjects with CGN and with accelerated hypertension. The mean serum levels of creatinine were as follows: primary CGN, 12.4 ± 8.3 mg/100 ml; accelerated hypertension, 14.4 ± 9.7 mg/100 ml; unclassified, 14.4 ± 11.2 mg/100 ml; and the miscellaneous group, 11.7 ± 7.3 mg/100 ml. There was no significant difference between these means (Table 4).

Discussion

Chronic renal failure is universally accepted as constituting an enormous health problem, with prevalence rates ranging from 25 to 100 per 10^6 population [10,12–14]. In the developing countries, the problem is compounded further by financial constraints, with the definitive treatment of either maintenance dialysis or renal transplantation being inaccessible to the majority of the subjects suffering from ESRD.

In this study we observed that CRF accounted for a staggering 8% of admissions, in contrast to 1.6% reported by Oyediran and Akinkugbe [7]. This could be explained by the prospective nature of this study, the selection factor, and the merging of both clinical and autopsy data.

It was observed that even though the clinical history was rather short in 39% of the subjects, a history of nocturia (at least twice per night) served as an indicator of the duration of the disease. It is, however, unfortunate that this most important symptom is not given due cognizance by our subjects.

Headaches with blurring of vision are very prominent features amongst our subjects with accelerated hypertension; this agrees with the experience of Seedat [9], Kincaid-Smith *et al.* [15], and Schottstaedt and Sokolow [16]. Few of these subjects seek competent medical advice and the majority take analgesics which could further aggravate the underlying chronic renal disease. Our subjects need to be educated as to the significance of these features.

Table 4. Table of clinical and biochemical parameters

Disease group	Clinical and biochemical parameters		
	Age* (years)	Diastolic blood pressure* (mmHg)	Serum creatinine* (mg/100 ml)
CGN	29.9 ± 12.9	115.8 ± 27.3	12.3 ± 8.3
Accelerated hypertension	33.1 ± 4.1	143.4 ± 13.6	14.4 ± 9.7
Miscellaneous	43.5 ± 13.5	106.6 ± 13.3	11.7 ± 7.3
'Unclassified'	42.3 ± 12.3	120 ± 15.1	14.4 ± 11.2

*All values represent mean ± standard deviation.

We observed that there was a predominance of males in our subjects with accelerated hypertension, in agreement with the experience in South African blacks [4,9], and in Caucasians [15–17]. It has been suggested that this predominance of male subjects could be due to differences in the latter part of life when hypertension in women runs a classically 'benign' course [15].

It is clearly recognized that severe hypertension is a common affliction amongst black populations [18,19]. In agreement with this, we observed that accelerated hypertension accounted for 25% of the causes of CRF among our subjects. Gold *et al.* [4] reported that accelerated hypertension was responsible for a comparably high percentage (33%) of ESRD in a group of 100 subjects. Akinkugbe [20] noted that seven out of 17 hypertensive subjects that came to autopsy had accelerated hypertension. Gold [21] observed that accelerated hypertension accounted for 39.2% of the subjects admitted for haemodialysis in a group of South African blacks.

The observation that accelerated hypertension is a predominant singular cause of CRF amongst the Negroid race is of epidemiological importance. Early detection and treatment of hypertension should therefore lead to a drastic reduction in the prevalence of CRF [22–24]. Unfortunately, however, the subjects with accelerated hypertension invariably present in hospital with advanced renal failure, at which time determination of the cause of the CRF may be clinically difficult.

This distinction is of paramount importance in the overall management of the subject, as control of the blood pressure determines, to a large extent, the prognosis. While blood pressure control may be achieved by rigid salt and fluid control and common anti-hypertensive drugs in the subjects with CGN, it may require very potent drugs, anti-renin agents and sometimes bilateral nephrectomy, in a proportion of subjects with accelerated hypertension, if optimum benefit is to be derived from kidney substitution/replacement therapy.

In this study, CGN is the leading cause of CRF, in agreement with reports from Africa [7,8] and elsewhere [2,10,14,25]. Note that the proportion of CGN amongst the subjects is relatively higher in the developing tropical countries than in the developed ones. A variety of infective agents has been implicated in the aetiology of CGN. These agents, *Plasmodium malariae*, filarial worms, hepatitis B virus, *Schistosoma mansoni*, *Mycobacterium leprae* and streptococcal organisms are present in endemic proportions in these areas and are conceivably responsible for the observed high prevalence of CGN. Control of these infections should lead to a reduction in the prevalence of CRF in the environment. We observed that chronic pyelonephritis (CPN) is not a significant cause of CRF in our subjects, and its rarity in this study is similar to the observation amongst South African blacks [4], Ugandans [5], Jamaicans [10], and Asians [25]. This contrasts sharply with the experience amongst Caucasians. In Scotland, CPN and CGN were of equal aetiological significance, being 29.6% and 27.6% respectively [26]. In Australia, Stewart *et al.* [12] observed that primary CGN and analgesic nephropathy contributed 31% and 39% to ESRD respectively, while hypertension accounted for only 6%, and vesico-ureteral reflux nephropathy 8%. In Brisbane [3], where analgesic abuse is common, pyelonephritis with papillary necrosis is the main cause of CRF, with primary CGN and accelerated hypertension accounting for a significantly low proportion.

A number of predisposing factors such as analgesic abuse, anatomical abnormality of urinary tract, and vesico-ureteral reflux have been implicated in CPN. These factors are notably rare amongst the Negroid race, and may thus account for the low prevalence of CPN in our subjects. Indeed, it is generally accepted that primary CPN is rare [3]. In agreement with this, Stewart *et al.* [12] observed that only four of their 403 subjects with CRF could be considered to have primary CPN in the absence of recognized predisposing factors. In an analysis of 173 subjects with CRF, Schechter *et al.* [27] also observed that CPN was usually associated with an underlying defect in the urinary tract.

Other rare causes of CRF amongst our subjects are, diabetic nephropathy, polycystic disease of the kidney and systemic lupus erythematosus. In view of the financial constraints, very few diabetic subjects live long enough to develop long-term complications such as renal failure. Other known causes of hypertension such as Conn's syndrome, phaechromocytoma

and fibromuscular dysplasia of the renal artery, which may lead to CRF, are also notably rare in Nigerians [28].

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