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Adult nephrotic syndrome in Ibadan, Nigeria: a prospective study of 135 cases

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Summary

One hundred and thirty-five adult patients admitted into the medical wards with the nephrotic syndrome have been studied over a period of 3 years.

The histopathology in eighty-one renal biopsies showed predominantly proliferative glomerulonephritis.

Nine patients had filariasis and in six of these the microfilaria isolated was *Loa loa*. Six patients had malarial parasitaemia; of these, three had *P. malariae* infection. Urinary schistosomiasis was diagnosed in four patients.

Twenty-seven patients were noted to be hypertensive and 104 patients had some degree of impairment of renal function. A total of nine deaths was recorded (6·7%) in the 3-year period.

The significance of these results is discussed.

Introduction

The nephrotic syndrome is an important cause of morbidity from renal disease in Ibadan, Nigeria. It is approximately ten times more common in local hospital practice than it is in Europe and America, accounting for 2–3% of all medical admissions into the adult wards of the University College Hospital (U.C.H.) Ibadan (Willis, personal communication 1965). It is, however, less significant a factor in renal mortality in this environment (Table 1). The purpose of this study is three-fold: to define the histopathology of adult nephrotic syndrome as seen in the wards; to assess the significance of malarial and microfilarial parasitaemia and urinary schistosomiasis, and to outline the role of hypertension, haematuria and urea retention in the overall prognosis of the disease.

Materials and methods

During the 36 months between January 1965 and December 1967, a total of 135 cases of the nephrotic syndrome were personally studied at the renal unit of the U.C.H., Ibadan. Practically all the patients seen were from Ibadan township (population 750,000) or the conglomeration of villages in its environs. Patients below 12 years of age and those suffering merely from massive proteinuria but without a substantial fall in their serum albumin levels were excluded from the study. Skin snips were taken for *Onchocerca volvulus* and *D. streptocerca,* blood was examined for the microfilariae of *Loa loa, D. perstans* and *Wuchereria bancrofti* and a minimum of three thick blood smears were taken for malarial parasites. In each patient, on at least two occasions, the urine was examined for the presence of ova of *S. haematobium*. Packed cell volume (PCV) was estimated by the microhaematocrit method and for the biochemical investigations the standard methods employed are as described in Varley (1962). Following intravenous pyelography, percutaneous renal biopsy was undertaken in ninety-three patients.

TABLE 1
Mortality from renal disease (U.C.H. 1965–66)

	No. of cases	Deaths	% mortality
Acute glomerulonephritis	24	12	50
Chronic glomerulonephritis	12	9	75
Acute pyelonephritis	19	5	26
Chronic pyelonephritis	50	16	32
Acute renal failure	9	7	78
Nephrotic syndrome	41	4	9·8
Miscellaneous (chronic renal disease)	10	6	60

Results

Of a total of 135 cases, sixty-four (47·5%) were male and seventy-one (52·5%) female. There were no patients over the age of 70 years. Over 80% were between the ages of 10 and 40 (Fig. 1).

Histopathology

In twelve of the ninety-three renal biopsies, the number of glomeruli present in the sections were too few to give conclusive results. The remaining eighty-one biopsies are analysed in Table 2. It is seen that proliferative glomerulonephritis accounts for the majority of cases. It must be stated that no attempt has been made to separate the proliferative into the generalized, localized, diffuse or focal (segmental) types (Dodge *et al.*, 1962), and although it is known that the prognosis varies as between the endothelial and predominantly epithelial varieties of proliferative nephritis, it has not been easy to distinguish numerically between these two. Fourteen cases showed thickening, splitting or duplication of the basement membrane component of the peripheral capillary wall as the dominant lesion. The miscellaneous group is further broken down to show pyelonephritis accounting for six cases (Table 3).

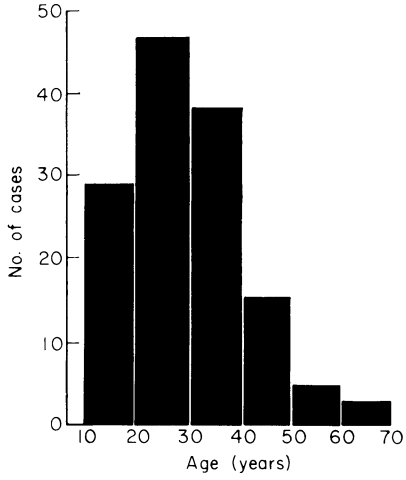

FIG. 1. Analysis of 135 cases of adult nephrotic syndrome (1965–67).

Protozoal and helminthic infections

The incidence of filarial infection and malarial parasitaemia is shown in Table 4. Microfilariae were detected in nine patients, two from skin snips (*O. volvulus*) and the rest from the blood. Loasis accounts for six (67%) of all the cases of filarial infection. In five of the six patients with loasis, eosinophilia was marked (over 10%). In no patient was *D. streptocerca* or *W. bancrofti* isolated from the sample taken.

There was a total of six patients with malarial parasitaemia. None of these was pyrexial at the time of taking the blood sample. Three of the six had quartan malaria, two tertian and in the sixth both *P. malariae* and *P. falciparum* were present in the thick blood smear.

The presence of urinary schistosomiasis was confirmed by the detection of ova of *S. haematobium* in the urine of four patients, all under the age of twenty-five years. Of these, only one had complained of antecedent haematuria.

TABLE 2

Histopathology of eighty-one cases of the nephrotic syndrome in U.C.H.

Minimal change	7
Membranous	14
Proliferative	35
Mixed (membranous/proliferative)	2
Chronic glomerulonephritis	9
Miscellaneous group	14

TABLE 3

Analysis of fourteen miscellaneous causes of the nephrotic syndrome in U.C.H.

Renal amyloidosis	3
Pyelonephritis	6
Toxic tubular necrosis	2
Diabetic nephrosclerosis	1
Renal vein thrombosis	1
Renal rickets	1

TABLE 4

Filarial infection and malarial parasitaemia in 135 cases of adult nephrotic syndrome

	No. of cases
Type of microfilaria	
O. volvulus	2
D. streptocerca	–
Loa loa	6
D. perstans	1
W. bancrofti	–
Type of malarial parasite	
P. falciparum	2
P. malariae	3
Mixed *P. falciparum*/*P. malariae*	1

Hypertension, haematuria and azotaemia

Hypertension was diagnosed when the recumbent blood pressure under basal conditions was 140/90 mmHg or over on at least two occasions. Using this criterion twenty-seven patients were hypertensive and of these, twelve were admitted in left ventricular failure. Eighteen of these hypertensive patients had renal biopsies and in thirteen there was evidence of proliferative glomerulonephritis with moderate arteriolar sclerosis. In the twenty-seven patients, eight had

had their illness lasting a year or more before seeking medical attention. Hypertension and the nephrotic syndrome were then diagnosed simultaneously. In five others, hypertension had supervened on a background of the nephrotic syndrome during several months of outpatient attendance.

In only two patients was a definite history of macroscopic haematuria obtained. These occurred about 15 months before the onset of the illness. Microscopic haematuria was subsequently detected in both these patients and in six more patients who were reported as having numerous red cells in the mid-stream urinary specimens.

The blood urea level was used as a crude index of glomerular function. A figure of 40 mg/100 ml was arbitrarily chosen as the upper limit of normal in this population (Edozien, 1958). Employing this parameter, 104 patients had some degree of renal impairment at one stage or another of their illness (Fig. 2). Thirty-eight patients had severe renal disease as shown by a blood urea of over 100 mg/100 ml. Of these, twelve were hypertensive. Histopathological studies could not be correlated with the degree of urea retention in these cases as intravenous pyelography, a desirable prelude to renal biopsy, could not have been rewarding.

A total of nine deaths occurred in the 135 cases (6·7%) during the 3-year period under study. Autopsy was carried out in eight, three showed changes of diffuse glomerulonephritis with epithelial proliferation, one membranous glomerulonephritis and one renal amyloidosis while in the remaining three patients the kidneys were small and scarred, with histological changes compatible with chronic pyelonephritis.

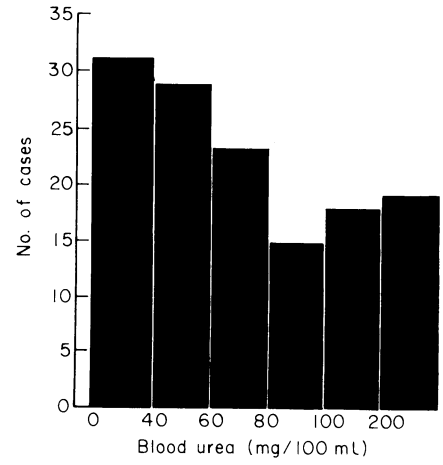

FIG. 2. Blood urea values in the nephrotic syndrome.

Discussion

The exact incidence of the nephrotic syndrome in the community at large still has to be estimated. It seems hardly surprising that there should be, as most authors have demonstrated, a disparity in figures for outpatient attendance, inpatient admissions and autopsy records in a disease complex characterized by a protracted course (Table 5).

The histopathological classification of the renal lesions in the nephrotic syndrome has always

TABLE 5

Renal disease in U.C.H. (data from five studies)

	Lauckner, Rankin & Adi (1958) Clinical: adult	Edington & Mainwaring (1958–62) Autopsy	Hendrickse & Gilles (1959–63) Clinical: paediatric	Akinkugbe (1965–66) Clinical: adult and paediatric in-patients	Akinkugbe (1965–66) Clinical: adult out-patients
Acute renal failure	—	10	—	11	—
Acute glomerulonephritis	9	2	22	24	—
Chronic glomerulonephritis	38	104	—	12	2
Acute pyelonephritis	4	12		18	3
Chronic pyelonephritis	2	51	7	49	29
Nephrotic syndrome	24	24*	156	65†	52
Miscellaneous	Unclassified	Amyloid 12 Ca kidney 10 Schisto, 7 Unclassified 20	Unclassified 11	Unclassified 14	Unclassified 27
Total number of cases	88	282	196	193	113

*Subacute glomerulonephritis.
†Includes detailed study of twenty cases.

been bedevilled by lack of uniformity in nomenclature. Thus, minimal change on light microscopy is grouped under the proliferative heading by some (Kibukamusoke & Hutt, 1967) whilst other workers prefer to classify it separately (Blainey *et al.*, 1960). Confused terminology is epitomized in the use of the word 'focal' as three different authors proffer separate meanings: Edington & Mainwaring (1966) using Dodge's classification (Dodge *et al.*, 1962) describe involvement of part of a glomerulus but Kibukamusoke & Hutt (1967) restrict the use of the term to abnormal involvement of some glomeruli, whilst others are spared. Spear (1965), however, denotes as focal, changes involving 'specific glomeruli and only specific tufts within an afflicted glomerulus—thus focal within the kidney and focal within the glomerulus'. It is with these difficulties in mind that we find ourselves unable to categorize the histological changes in our specimens any further than as essentially minimal change, and as proliferative and membranous glomerulonephritis. It must be stated that the majority of cases of proliferative nephritis were of the localized diffuse variety. It is also noteworthy that these appearances differ somewhat from those classically found in children in the same environment. Hendrickse & Gilles (1963) and Edington & Mainwaring (1966) describe biopsy findings in children in Ibadan with the nephrotic syndrome as falling into two main groups: the localized focal proliferative (simulating post-streptococcal nephritis) and the localized focal membranous. Both groups of workers agree that diffuse membranous changes are extremely rare in this environment.

Filariasis was noted in nine of the 135 cases and the majority of those so infected turned out to be loasis. A significant link has been recently contested, on both epidemiological and immunological grounds between endomyocardial fibrosis and loasis (Ive *et al.*, 1967). Our figures are too small to draw any valid conclusions as to the causal relationship between loasis and the nephrotic syndrome in the tropics. It is possible that any relationship between these two conditions is fortuitous.

Nearly 40 years ago, a striking association was emphasized between the occurrence of massive proteinuria and *P. malariae* infection (Giglioli, 1930). The same worker subsequently went on to prove (Giglioli, 1962) the virtual disappearance of the nephrotic syndrome with eradication of malaria in Guyana. This relationship has been amply confirmed in childhood nephrosis in both West and East Africa (Gilles & Hendrickse, 1960; Hendrickse & Gilles, 1963; Kibukamusoke, 1966b). The same association has been suggested in adults in East Africa by Kibukamusoke (1966b). It has been suggested that the antigenic response to infection by *P. malariae* 'sets the stage' for vulnerability of the glomerulus to a wide variety of potentially toxic agents. A limited study of eleven patients by Kibukamusoke (1966a) in Lagos, Nigeria showed the presence of *P. malariae* in seven adult nephrotics as compared to only two in controls. Whether the same association can be proved in adults with the syndrome in West Africa remains a matter for speculation but our present results do not point in the affirmative. It is, of course, possible that the initial renal damage occurs during infection with *P. malariae* in childhood, leaving a legacy of proteinuria that becomes obvious in later years, long after the malarial parasitaemia has disappeared.

Since Gelfand (1963) reported fifteen cases of urinary schistosomiasis in twenty-five consecutive African subjects with the nephrotic syndrome in Central Africa, some attention has been focussed on a possible aetiological relationship. We can find no grounds for this in the present series. Only four of our 135 patients had urinary schistosomiasis, an incidence no higher than one would expect in the rest of the population, for Ibadan is a well-known endemic area for urinary schistosomiasis (Cowper, 1963).

The incidence of hypertension in this series was 20%. Majority of the hypertensives showed evidence of proliferative glomerulonephritis. It is notable that a number of these patients developed hypertension after about a year's follow-up as known cases of the nephrotic syndrome; others admitted to an antecedent history of insidious oedema for about a year before the nephrotic syndrome and hypertension were simultaneously diagnosed. Urea retention of some degree was present in 77% of all cases of the nephrotic syndrome. This seems a higher figure than that of Kibukamusoke (1967) who in a study of fifty-one cases of the nephrotic syndrome found a 'significant degree of urea retention' in twenty-eight. It appears remarkable that the mortality from this illness for the period under review was so low (6·7%) when one considers that thirty-eight patients had blood urea values of over 100 mg/100 ml and twelve of these (31·6%) had coincident hypertension.

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