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CHRONIC RENAL FAILURE IN NIGERIA: THE TRIALS AND TRIUMPH

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CHRONIC RENAL FAILURE IN NIGERIA: THE TRIALS AND TRIUMPH

Mr Vice Chancellor Sir,

It gives me great pleasure to deliver this inaugural lecture which is long overdue but has had to wait for specific targets to be attained - triumph after a long period of trials in the challenging and engaging nephrology landscape. But no sooner than apparent triumph was achieved than more daring challenges crept in. The title of this inaugural lecture **'Chronic Renal Failure ; The Trials and Triumphs'** is informed by the growing concern of the entire world for the devastating effects of this condition which has become a public health priority. The media (print, electronic) is awash with appeals for financial assistance for young people in their economically productive years for kidney transplantation.

My academic and professional careeer commenced at the feet of Prof OO Akinkugbe, my teacher and mentor, at the University of Ibadan, from whom I have continued to draw a great inspiration. A spell at Guy's Hospital London under Prof Gwyn Williams ignited in me a deep passion for investigative and laboratory research in immunology of glomerulonephritis. Great physicians such as Prof OO Osuntokun, AA 'Adetuyibi and A Iyun of blessed memory had significant impacts on me.

Introduction:

Chronic renal failure (CRF) can be defined as a persisting and progressive deterioration of renal function leading to increasing retention of waste products of metabolism and a consequent disturbance of the body's internal milieu. By the simple parameter of serum creatinine the levels are consistently above 174.6μmol/1 or a GFR of 60ml/min at least for 3 months[1,2].

In recent times, emphasis has shifted to a more encompassing terminology "chronic kidney disease" which includes kidney disease manifesting as

structural kidney damage with/without a reduction in GFR, or functional kidney damage with reduction in GFR (Table 1).

Table 1 : Definition of Chronic Kidney Disease (CKD)[2]

1.	**Kidney damage for 3 months , with or without decreased GFR, as manifest by either:**
	▪ **Pathologic abnormalities; or**
	▪ **Markers of kidney damage, including abmormalities in the composition of the blood or urine, or abnormalities in imaging tests**
2	**GFR < 60ml/min/1.73m² for 3 months with or without kidney damage.**

Table 2 : Magnitude of Chronic Kidney Disease (CKD)

Stage	Description	GFR ml/min/1.73m²	US Prevalence, 1000s	US Prevalence, %
1	Kidney Damage with normal or increased GFR	≥ 90	5900	3.3
2	Kidney damage with mildly decreased GFR	60 - 89	5300	3.0
3	Moderately decreased GFR	30 - 59	7600	4.3
4	Severely decreased GFR	15 - 29	400	0.2
5	Kidney Failure	<15	300	0.1

Five stages have been identified [Table 2]. This new approach is borne out of the profound morbidity and mortality associated with the condition even in apparently healthy individuals, well before the development of recognized clinical features of uraemia. CRF has emerged as a public

health priority as it is assuming epidemic proportions all over the world I shall address the problem of chronic renal failure from the perspectives of the challenges it poses in its aetiological factors, its prevention; control and management as derived from our research and clinical endeavours. I will highlight what the many trials there have been and the modest triumph with a view to charting a direction for policy and research strategies for sustainable control and management of this epidemic[2].

CRF poses serious medical, social and economic problems with respect to the enormous cost of prevention and management all over the world. The problem is spectacular in Nigeria and indeed Africa in view of the several inherent factors.

- An undeveloped economy and infrastructure,
- Low level of technology and
- Environmental and social and cultural factors
- Poor access to healthcare. [Table 2].

MAGNITUDE OF THE PROBLEM:

Inspite of the consensus that chronic kidney disease with its attendant complication CRF is very prevalent in Nigeria and indeed indigenous Africans, only data from hospital centres are available. These are grossly incapable of providing valid information for effective planning. It is common knowledge though, that CRF is the 3rd commonest cause of death among Nigerian adults, while its incidence and prevalence are virtually unknown. Data generated from hospital centres agree to a high occurrence of treated CRF with figures ranging from 2—8% of medical admissions[3,4].

Table 3: Survey of CRF in Tertiary Centres

CRF as a proportion of medical admissions				
No of Centres	2	6	2	
% Medical Admissions	<2	2-4	>4	
Number of patients per year				
No of Patients	100-120	50-60	25-30	10-15
Duration of	>2 wks	1-2 wks	½ wk	¼ wk
No of Centres	6	3	-	1
Sex Distribution				
Distribution	M>F	M=F	F>M	
No of Centres	9	1	-	
Highest proportion in age group				
Age group	11-20	21-30	31-40	41-50
No of Centres	-	3	5	2
Highest proportion in socio-economic status				
Socio-economic status	High	Middle	Low	
No of Centres	-	4	6	

Our limited survey [Table 3] of tertiary and specialist hospitals in the country has since confirmed this. Ten centres out of 16 surveyed responded to our detailed questionnaire. CRF accounted for between 2 and 4% of medical admissions in 6 centres, above 4% in 2 centres while it fell below 2% of medical admissions in 2 centres. In 6 centres between 100-120 new cases were seen per year while 3 centres saw 50 – 60 patients per year, and in 1, 10 – 15 were seen per year. On the average, 1 – 2 new cases

were seen per week, with an estimated total of 1000 cases per year seen in the 10 centres[3].

These data are revealing as by extrapolation on population figures, we obtained a prevalence of about 400 per million. But they cannot substitute for actual prevalence derived from community survey.

In countries with efficient renal registries, the incidence and prevalence data are very reliable. Poor infrastructural facilities hamper the development of national registries in Nigeria. This is compounded by the fact that an insignificant proportion of patients ever gets to any hospital, while yet fewer report to the tertiary centres. Hospital incidence of CRF will thus grossly underestimate the magnitude of the problem. There is a need for a community-based survey of CRF in Nigeria for a valid appraisal of the size and rational healthcare prioritization in this country.

In the USA, the prevalence of CKD obtained from a longitudinal community based study of 15626 participants is 11% (translating to 19.2 million adult population with those in CKD stages 3 – 5 constituting about 4.7% (8.3m)[5]. In the UK, the prevalence of CKD (stages 3 – 5) is 5.1%[6], while in Australia the prevalence of CKD (stages 3 – 5, (those with GFR<60 ml/m) is 11.2%[7]. In a Singapore survey, a prevalence of 5.1 – 8.0% of the population had CKD as defined by presence of significant proteinuria and or haematuria[8]. The differences observed in the various prevalence rates of CKD are also noted in the occurrences of ESRD in the various populations. [Table 4][9].

Table 4: Prevalence of ESRD in various populations

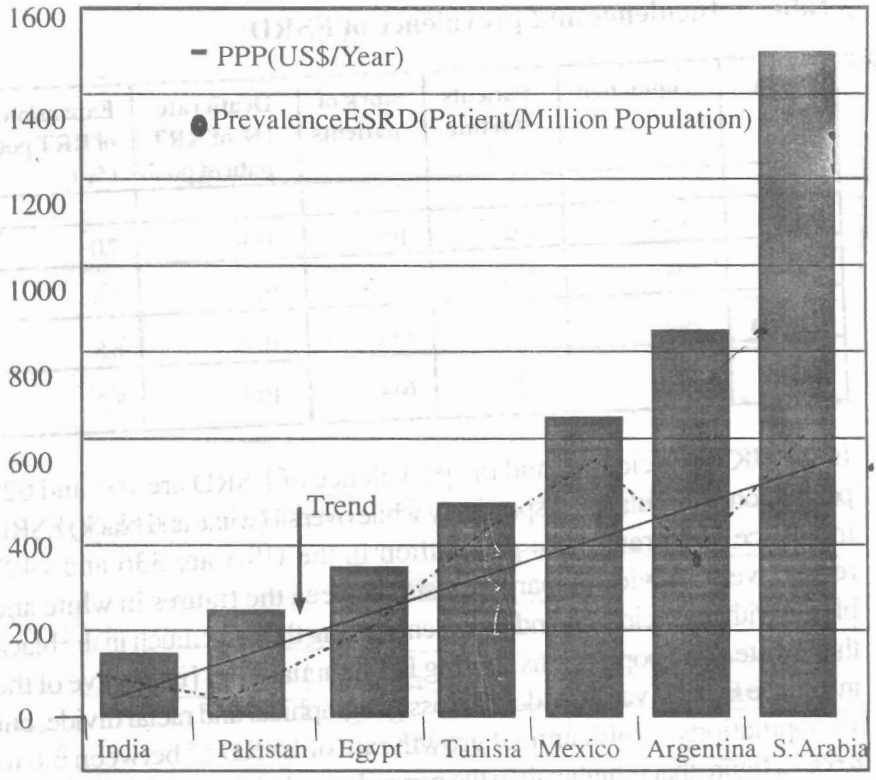
Country Population	Incidence of ESRD per million per year	Prevalence of ESRD per million per year
Europe		
UK	101	626
European Average	135	700
Russia	15	79
Australia		
White people	94	658
Aboriginal people	420	1895
USA		
Overall	336	1403
White People	256	1004
African - American	982	4432
Less Developed Countries		
India	34-240	Unknown
Nigeria	Unknown	2.5
Most data are from the period 2000-2003 (El-Nahas & Bello, 2005)		

Table 5: Incidence and prevalence of ESRD[10].

Country	Population	Patients starting RRT	Stock of patients	Death rate (% of RRT patient pool)	Expansion of RRT pool (%)
USA	262.8	262	101.3	18.9	7.0
Japan	125.6	210	1230	9.3	7.8
Canada	29.6	104	613	10.4	6.6
EU	372.6	120	644	10.4	8.2

In the UK the incidence and the prevalence of ESRD are 105 and 625 per million of population respectively while overall (white and black) ESRD incidence and prevalence per million in the USA are 336 and 1403 respectively. A wide disparity exists between the figures in white and blacks with the incidence and prevalence being thrice as much in the black than white. The populations starting RRT annually i.e. [indicative of the incidence ESRD] varies widely across geographical and racial divide, but all populations exhibit annual growth rate of ESRD of between 6.6 to 8.6% (a figure that is higher than the general population growth rate) (Table 5). Data from the developing countries are unreliably low, though they reflect lack of renal registries and poor access to RRT. Indeed there is a strong relationship between the gross national product and availability of renal replacement therapy (Figure 1)[10].

Fig 1: Discrepancies in the rate of RRT Vs Purchasing Power Parity:



Culled from USRDS Annual Data Report[10]

In 2005 more than 1.6m people were on dialysis globally, with 90% of these being in the developed world. This is projected to increase to 2.5 million by 2010, a 7% increase every year. In 112 countries with a population of about 600 million especially Africa, little or no RRT exists. 1.0 million ESRD patients die every year[10].

The cost of renal replacement therapy and total renal care is enormous, and constitutes about 2% of the medical budget in the UK for less than 0.1% of the population. In the USA, the current annual cost of RRT is

US$ 22.8 billion and it is expected to rise to US$ 29.0 billion by 2010. The global cost estimate is put at US$ 1.0 trillion in a decade from year 2000[10].

CRF poses yet another socio-economic problem as it affects more males than females mostly in age bracket 20 – 40 years the most economically productive years. Our own data both from a local study and survey of tertiary specialist centres clearly confirmed this. The highest proportion of patients was in age group 21 – 30 years in 3 centres; 31 – 40 years in 5 centres; and 41 – 50 years in 2. Majority of the patients were of low socio-economic status and had a maximum of secondary school education[3]. This picture is comparable to experience in India, Pakistani and other African countries.

ETIOLOGICAL CONSIDERATIONS:

Crucial to prevention of CRF is a good knowledge and understanding of its causes. Our studies and others have identified chronic glomerulonephritis (CGN) and hypertensive nephrosclerosis (HTN) as the leading causes of CRF in Nigerians (Table 6)[1]. Diabetic nephrosclerosis, hitherto a rare cause, was ranked as the 3rd leading cause of CRF by a majority of centres in our survey. Obstructive uropathy and hereditary renal disease were gaining importance while chronic atrophic pyelonephritis still remains insignificant. Inspite of the large consumption of analgesics and herbal concoction and the high prevalence of sickle cell disease and hydrocarbon pollution with gas flaring not much exists on their etiological importance in CRF in Nigerians.

Chronic Glomerulonephritis

Chronic Glomerulonephritis (CGN) is a leading cause of end-stage renal disease in Nigeria, accounting for about 50% of the cases. (Table 6).

Despite the relatively common nature of the disease, the basic cause in the majority of adult patients remains unknown.

Table 6: Pattern of Disease and method of diagnosis				
	Method of diagnosis			
Disease group	Clinical	Biopsy	Autopsy	Total
Chronic Glomerulonephritis	31	11	8	50
Accelerated Hypertension	20	-	5	25
Miscellanous	3	2	4	9
Unclassified	16	-	4	16

There is however a tendency to lump all cases together as tropical nephropathy – a rather ill-defined term, deriving largely from the suspected role of the plethora of infective agents that abound in the tropics.

Identification of specific agent(s) would render them amenable to control measures, with appreciable impact on the prevalence of the disease and on the disease process.

Hard scientific data on cause-effect relationships are difficult to come by in tropical practice, and, only associations between aetiological factors and chronic GN are generally available except in a few published works.

We have over the years conducted a series of studies to identify or at best to incriminate some putative agents in the cause/aetiopathogenesis of the disease. Our studies have provided some evidence for the role of (i) Hepatitis B antigen (ii) Filarial loa loa, (iii) Hydrocarbon (Petroleum), (iv) malaria parasite (v) HIV in the etiology or development of CGN. The contribution of Sickle Cell Haemoglobin, IgA nephropathy or Lupus erythematosus has been remarkably insignificant.

The search for the etiology of CGN presents a daunting challenge to the nephrologists in the tropics, inspite of the general notion that most of the cases are post-infectious GN. Even then, its control, and prevention will rest mainly on the understanding of its immunopathogenesis. Central to

this is the host-parasite interactions. These lead to a variety of complex adaptive immune responses fundamentally aimed at host's survival, they are triggered primarily by the recognition of foreign parasite antigens in the context of the host's major histocompatibility complex (MHC) coded antigens. A variety of ill-defined parasite antigens located on the surface membranes of the parasite and metabolic antigens – such as excretory are exposed to the host. They are recognized by the host's immune cells (macrophages/leukocytes/endothelial cells) and in turn provoke certain immune responses. These include.

- Formation of antibodies which include non-specific and auto reactive antibodies;
- Formation of immune complexes (IC) in circulation or in situ in the kidney;
- Activation of polymorphs, lymphocytes and interaction between macrophages/monocytes with production of mediators of injury including lymphokines (interleukins) and other growth factors.

The effects of these on resident cells in the kidney manifest as nephropathy. However, elucidation of the pathways involved in specific categories of post infections GN has been made difficult in Nigeria by inadequate laboratory and other research facilities. Treatment of the suspect organism offers little benefit if any, except perhaps in the early cases. Treatment is now directed at interfering with the immunogenetic pathway by employing anti-inflammatory / immunotherapeutic agents such as cyclosporin, Mycophenolate mofetil and monoclonal antibodies to interleukins etc. Furthermore, militating against control of post infectious nephropathy includes the following:

- ✓ Lack of adequate data on the prevalence of the disease;
- ✓ Lack of specific diagnostic criteria, and
- ✓ Lack of adequate knowledge of the specific nephritogenic antigens of the organisms.
- ✓ The interactive effects of other infective conditions and malnutrition in the modulation of immune response.

Hepatitis B antigenaemia

The association between Hepatitis B virus (HBV) infection and glomerular diseases was first reported in 1971 and various morphological patterns including membranous nephropathy, mesangiocapillary GN and minimal change nephropathy have been reported (Combes et al 1971[11], Brosko et al 1974[12]). A close aetiopathogenetic association has been demonstrated by Lai et al[13], through the presence of glomerular deposits of Hepatitis B surface Antigen (HBsAg), Hepatitis B core Antigen (HBcAg) and both (HBsAg and HBcAg) in a significant proportion of patients with IgA nephropathy.

Post infections GN is the predominant type of GN in Nigerian practice: the histological pattern of Mesangioproliferative and mesangiocapillary GN are as common as in the cases of Hepatitis-associated IgANephropathy reported by Lai and others[13], thereby suggesting the possibility of a novel pathway, yet unrecognized, for HepatitisB induced GN in our environment.

We sought the role of Hepatitis B virus in the chronic glomerulonephritis in our patients (Table 7) [14]. Eighty one adult patients with chronic GN and who had not been on dialysis were tested for Hepatistis Bs antigenaemia. The distribution of the clinical diagnosis is as follows: 9 asymptomatic proteinuria, 39 nephrotic syndrome and 33 azotaemia with profuse proteinuria (Table 8). The histopathology as obtained in 40 showed 22 with MCGN, 4 FSGS, 3 Proliferative GN, 1 Minimal Change and 10 ESRF (Table 9). None had apparent clinical evidence of liver disease or history of jaundice. The prevalence of Hepatitis Bs antigenaemia was 33.3% (cf 6% in normals). The prevalence was higher in groups with nephrotic syndrome and asymptomatic proteinuria than in the group with advanced renal failure. Bs antigenaemia was found in all histological forms, but most prevalent in the MCGN ($p<0.001$)[14].

Table 7: Comparison of Prevalence of hepatitis B_s Antigenaemia Between Patients and Controls				
Population	**n**	**Number with hepatitis B_s Antigenaemia**	**Percentage**	**Level of Significance (P)**
Normal Controls	180	11	6%	P<0.001
Patients with chronic glomerulonephritis	81	27	33.3%	

Table 8: The Pattern of Clinical Diagnosis with respect to hepatitis B_s Antigenaemia			
Clinical Diagnosis	**Number of Patients**	**Number with hepatitis B_s Antigenaemia**	**Percentage**
Asymptomatic persistent proteinuria	9	4	44.4
Nephrotic Syndrome with serum creatinine < 3mg%	39	16	41.0
Gross proteinuria with hypertension and serum creatinine ≥ 3mg%	33	7	21.2
Total	81	27	33.3

Table 9 : Histopathologic pattern in patients with hepatitis B_s Antigenaemia			
Histopathology	**Number of Patients**	**Number with hepatitis B_s Antigenaemia**	**Comparison of Prevalence In Normal Control – Level of Significance**
Mesangiocapillary glomerulonephritis	22	11	<0.01
Focal glomerulosclerosis	4	1	-
Proliferative glomerulonephritis	3	1	-
Minimal Change glomerulonephritis	1	1	-
End stage Kidney (Autopsy)	10	1	>0.5

Filariasis & Glomerulonephritis

Some filarial worms (particularly *Loa Loa*) have been incriminated in the aetiology of nephropathy in the tropics. Loaisis is an helminthic infection caused by the filarial worm, Loa Loa, transmitted by Tabanid flies. It is endemic in Equitorial West and Central Africa. Pillay, Kirch and Kurtzman[15] reported Loiasis associated GN in Nigerian students in USA, while Ngu et al[16]. identified Loiasis in 10 patients with GN in the neighbouring Cameroon. The common renal histopathologic forms seen were Proliferative GN and membranous GN. They demonstrated specific antibodies with corresponding antigens in serum and glomeruli of patients. A prolific production of specific antibodies were also identified. These include: i) cross-reactive antibodies to glomerular antigens – laminin, collagen IV and heparan sulphate. This is due to the presence of parasite antigens – filarial proteoglycan-bearing antigenic determinants such as Phosphorylcholine and cuticular collagens which may share antigenic

determinants with the host tissue components and ii) autoantibodies such as antiDNA, antiRheumatoid factor resulting from polyclonal B cell activation[17].

In an attempt to define the role of filariasis in our patients with chronic glomerulonephritis, we carried out a clinicopathologic study of 66 patients (38 GN with filariasis, 28 GN without filariasis) and controls being filariasis alone (without GN, and healthy patients)[18].

The renal histopathologic pattern is as shown in table 10. Both groups (GN with and without filariasis) showed mostly focal glomerulosclerosis, mesangioproliferative GN and mesancaprildary GN types, with no clear distinction between them.

Table 10: Renal Histological Pattern in Patients.

Histopathology	Filariasis + GN	GN without Filariasis
Minimal Change GN	1	4
Focal Segmental glomerulosclerosis	5	8
Diffuse Proliferative GN	12	3
Mesangioproliferative GN	4	4
Mesangiocapillary GN	5	1
Membranous GN	1*	1
Chronic GN	6	5
Clinical "Chronic GN"	6	5

* - Mixed membranous + proliferative changes

However, there was a fewer number of patients with minimal change GN in the filariasis group than the non-filariasis group. We were particularly

impressed by the presence of microfilaria worms in the glomerular tuft and interstitium of some of the patients (Figures 2-5)[18,19].

Fig 2: Microfilaria within Glomerulus with thickening of glomerular capillary wall and hypercellularity (Mixed membranous and proliferative GN)

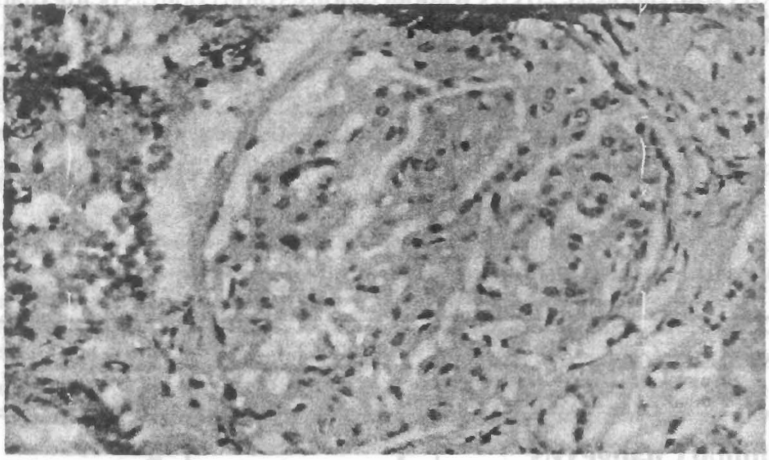


Fig 3: Microfilaria in the interstitium, adjacent to it is Glomerulus showing hypercellularity

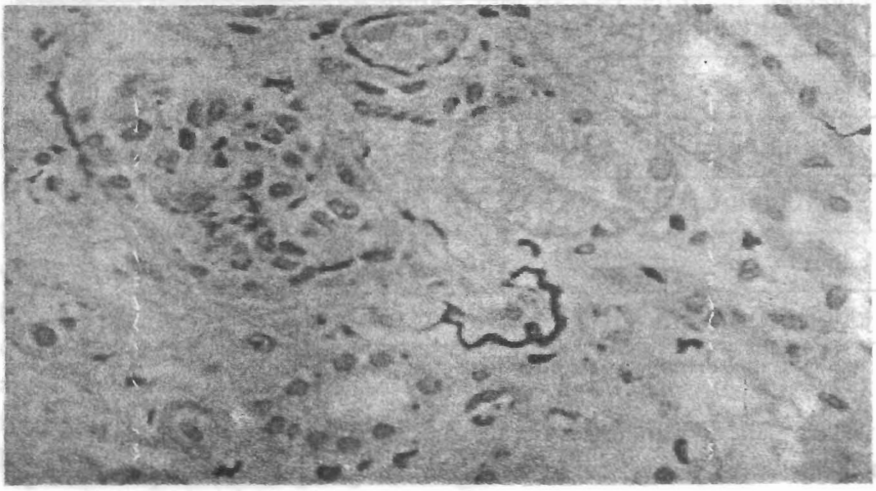


Fig 4: Cross section of Microfilaria within the Glomerulus showing features of Focal (proliferative) Changes.

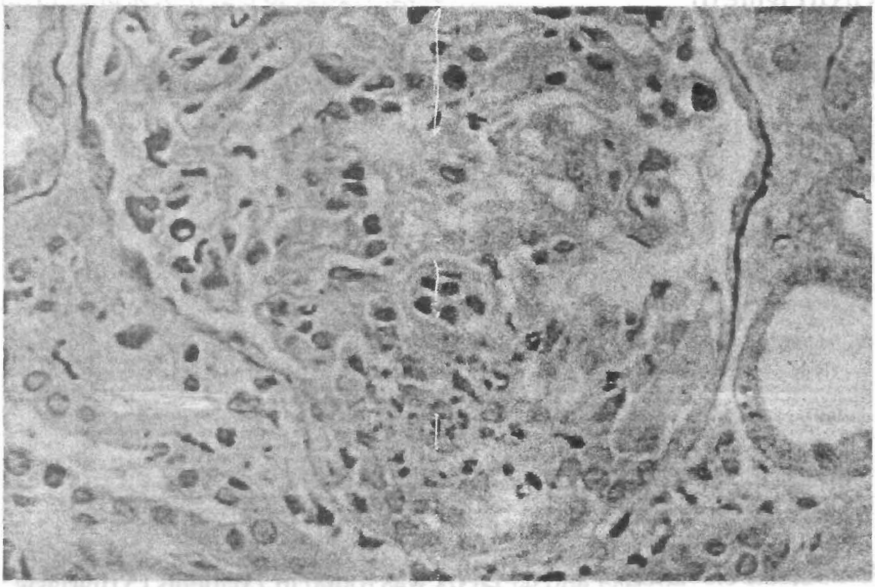
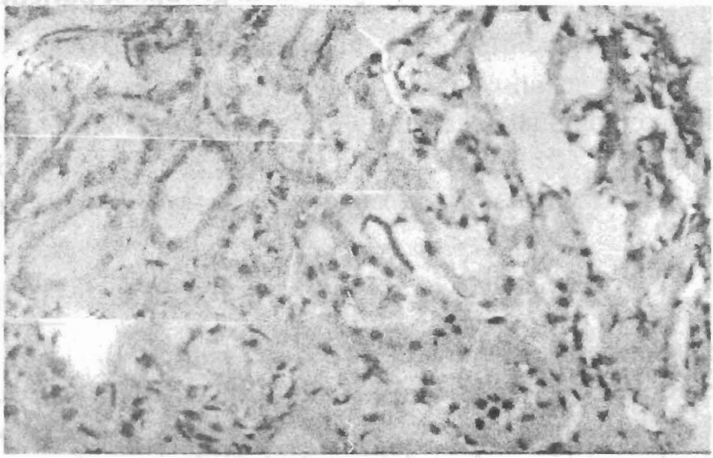
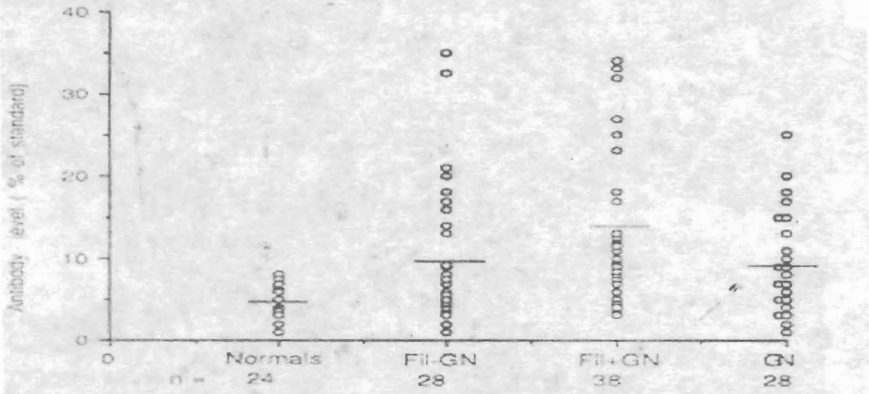


Fig 5: Microfilaria in the Tubules



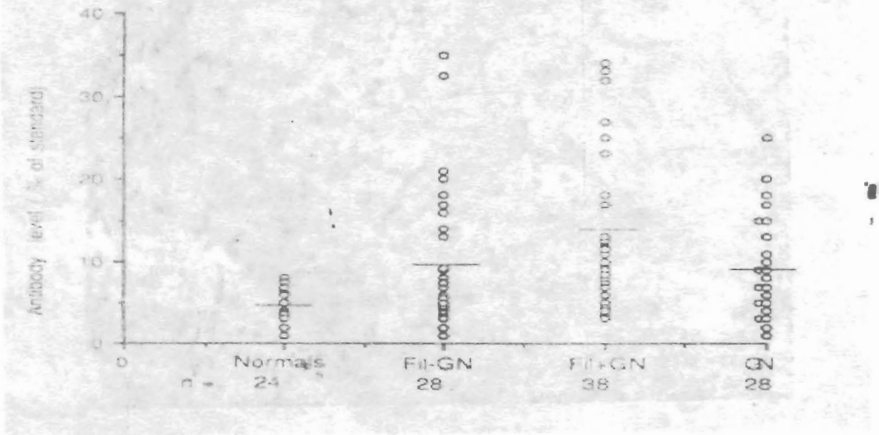
We also demonstrated a production of auto antibodies in filariasis irrespective of the presence of GN. Mean IgG anti SS-DNA antibodies were elevated in filariasis (22 out of 38 with GN) and 13 out of 28 without GN) (Figure 6)[19].

Fig 6: IgG antiss – DNA antibody levels in groups of patients



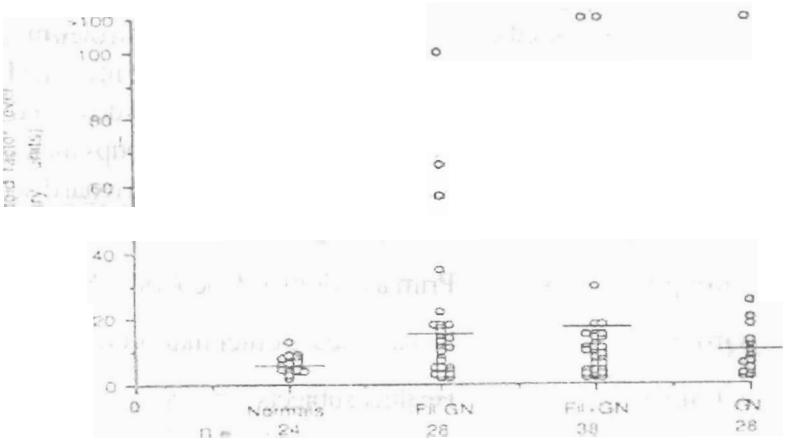
A moderate elevation of anti ds-DNA was found in 7 patients [5 filariasis with GN and 2 without GN) (Figure 7).

Fig 7: IgG antids – DNA antibody levels in groups of patients



Rheumatoid factor isotypes (GM) were significantly increased in the Loiasis patients and Loiasis with GN (there was no correlation between these levels and serum IgG or IgM (Figure 8)[19].

Fig 8: IgM Rheumatoid factor levels in groups of patients



Anti-Laminin antibodies were significantly higher in Loiasis patients with GN and without.

The presence of these auto antibodies could result of (i) cross-reactive antibodies to glomerular antigens – laminin, collagen iv and heparian sulphate. This is due to the presence of parasite antigens such as phosphorylcholin and cuticular collagens, which share antigenic determinants with host tissue components. (ii) activation of polyclonal B cells.

HYDROCARBON & GLOMERULONEPHRITIS

There is a body of data derived from animal experimentation and observations on humans pointing to a possible association between Hydrocarbons (HC) exposure and development of renal disease. In vitro stimulation of mesangial cells by Benzo{a} pyrene, a widely used polycyclic

Hydrocarbon resulted in proliferation of the cells while exposure of laboratory animals lead to glomerular damage[20,21].Lesions similar to Goodpasture's syndrome and proliferative GN with focal glomerulosclerosis have been reported in experimental animals while various clinical groups have reported a significantly greater exposure to HC in patients with GN compared to control groups. It was imperative that the role of Hydrocarbons in glomerular disease in Nigeria be defined in view of the leading position of Nigeria as a world producer of crude petroleum and the wide and uncontrolled exposure of her citizens to petroleum and petroleum products. We therefore compared a quantitative life time HC exposure among 3 groups of subjects using an instrument designed by Yaqoob et al [22], with slight modification (Table 11). The groups included (i) patients with Primary glomerulonephritis, (ii) patients with renal disease other than primary GN and (iii) healthy subjects as indicated below:

- Group 1 - Primary Glomerulonephritis (1 GN)
- Group 2 - Renal disease other than 1 GN
- Group 3 - Healthy subjects
- Instrument for assessment is as given below:

Table 11: Assessment and grading of hydrocarbon exposure scores.

SOURCES OF EXPOSURE	INTENSITY FACTOR	Duration of Exposure				
		HOURS PER DAY	DAYS PER WEEK	WEEKS PER YEAR	TOTAL NO. OF YEARS	SCORE
House painting indoors	2					
Glue Sniffing	2					
Spay-Painting without Protection	2					
Carpet-Cleaning agents	2					
Paints and glue production	2					
Spray-Painting with protection	1					
Printing work	1					
Anaesthetic work	1					
Dry Cleaning	1					
Use of Pesticides	1					
Hairdressing chemicals	1					
Greasing/degreasing	1					

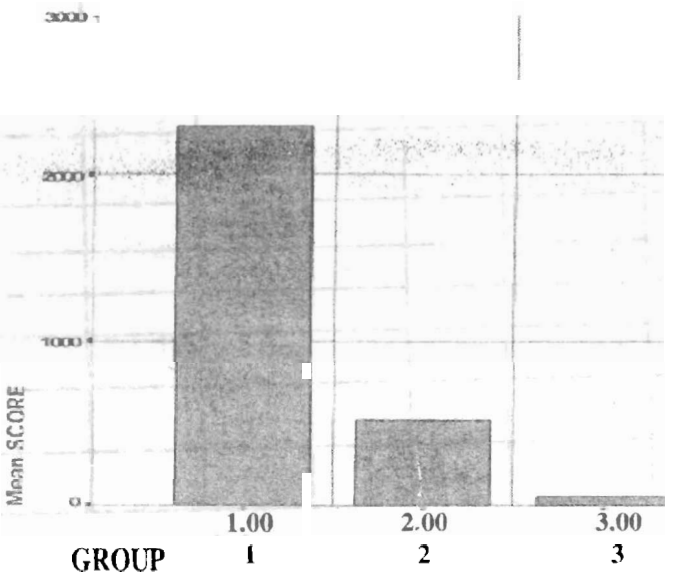
Exposure score= Total No.of Exposure Hours X Intensity factor

Mean HC exposure was significantly higher in group 1 (i.e patients with primary GN) than in the other groups. A higher proportion (45%) of subjects in that group (Group 1) had exposure scores above the 75 percentile, compared to 25% in the controls (Table 12; Figures 9 & 10).

Table 12: Table of Mean Hydrocarbon Exposure Scores

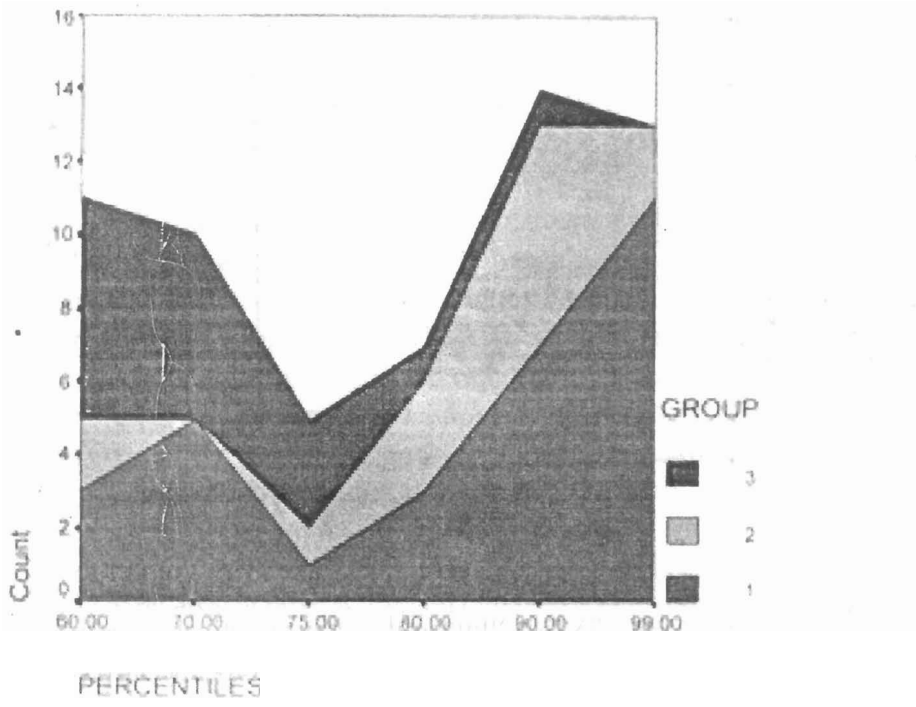
	Group 1	Group 2	Group 3
Mean exposure Scores Mean ± SD (range) X^2=11.825;p= 0.003	2295.81 ± 4945.76 (0 – 24,000)	501.83 ± 1338.66 (0 – 7020)	53.44 ± 110.75 (0 – 502)

Figure 9: Bar Chart Showing mean hydrocarbon exposure scores for each of the three groups.



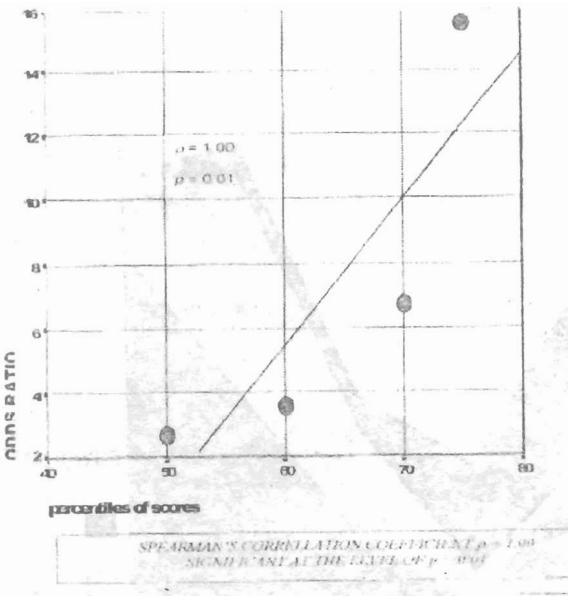
$X^2 = 11.825,$ P=0.003

Figure 10: Area Chart Showing the distribution of exposure scores among the groups – Demonstrating the predominance of group 1 cases in higher percentiles.



The odds ratio (OR) for the risk of CRF from primary GN showed a steady increase with Odds Ratio leaping from a value of 2.1 (for exposures scores of up to the 50th percentile) to an Odds Ratio of 15.57 (for exposure scores of up to the 75th percentile) (Figure 10) [22]. There is a positive correlation between the risk of primary GN and exposure score ($r = 100$, $p<0.001$, Fig. 11).

Figure 11: Graph showing Correlation between odds ratio of developing GN and hydrocarbonexposure scores percentiles.



These findings are very intriguing as they have political, economic and health implications. Our recommendation is that vigorous health promotion campaigns should be mounted in the petroleum producing areas, while more rigorous scientific studies be commissioned by government.

Human Immunodeficiency Virus Associated Nephropathy (HIVAN):

It is only in recent times that Human immunodeficiency virus became well associated with nephropathy (HIVAN) with it being first described in 1984 among intravenous, heroin abusers with AIDS[25]. HIVAN can occur in people with HIV infection or those with the full blown AIDS. It is important as HIV pandemic is assuming unmanageable proportions in this country with the prevalence rate being between 5-7% rising up to 15% in some

parts of the country, in adult Nigerians and 10% of whom may develop HIVAN. It is the 3rd commonest cause of ESRF in blacks in New York City, and has a male predominance. HIVAN is manifested by heavy proteinuria (but relatively less impressive peripheral oedema) and renal insufficiency; it is characterized by the presence of collapsing variant of focal and segmental glomerulosclerosis with tubular necrosis and significant interstitial inflammation. It runs a rapidly progressive course reaching ESRD within 4-6 months. The kidney size is relatively preserved and may be large, and is readily demonstrable and hyperechoic on ultrasonography. Characteristic histologic features include wrinkling and collapse of the capillary wall in the affected glomerula with narrowing and obliteration of the capillary lumen, and dilatation of the Bowman's space and a prominent lack of mesangeal proliferation .There is excessive interstitial fibrosis and microcytic dilatation of the tubules. There is positive staining for IgM and C3 in the sclerotic tissues. Electron microscopy reveals deposits of intraendothelial tubuloreticular structures. The pathogenosis is by direct injury of HIV or its proteins to the renal epithelium and the stimulation of gene products – TGF-b and basic fibroblastic growth factors, with consequent sclerotic and fibrosing process. Treatment with highly active antiretroviral regimen, steroids and ACEI have proven benefits with remission or reversal of progression and improvement in serum creatinine levels and reduction of proteinuria[24,25]. Our search for the role of HIV in chronic kidney disease in Nigerians has been recently published[26].

In a clinicopathologic study of 400 consecutive HIV seropositive patients, we observed a high occurrence of renal disease (albuminuria and/or elevated serum creatinine) most probably attributable to HIV infection in 38% (male to female ratio of 1.0 to 1.06), with significantly low serum albumin and total cholesterol in 45.5%. A high proportion of 8.8% had reached ESRD. Marital status, malnutrition and severity of infection as reflected in the low CD4 count, seem to promote the development of nephropathy.

Table 13: Risk factors for renal dysfunction in HIV positive patients.

VARIABLES		HIV PATIENTS with renal dysfunction	HIV PATIENTS without renal dysfunction	P-value
MARITAL =	SINGLE STATUS	50	77	0.994 (X2 value 0.77)
	MARRIED	78	129	
	DIVORCED	8	13	
	WIDOWED	16	29	
EDUCATIONAL	NONE	4	13	0.423
	STATUS PRIMARY	44		60 (X2 value
	SECONDARY	76	130	= 3.875)
	POST-SECONDARY	28	45	
Age (years)		36.6 ± 10.3	34.2 ± 9.1	0.016
BMI (kg/M2)		18.5 ± 3.1	20.02 ± 3.5	0.000
Systolic BP (mmHg)		115.43 ± 21.81	117.01 ± 16.03	0.428
Diastolic BP (mmHg)		75.02 ± 12.84	75.03 ± 11.18	0.994
CD4 Count (cells/iL)		253.3 ± 191.8	320.4 ± 237.7	0.022
PCV %		25.33 ± 7.19	29.82 ± 6.98	0.000
Serum total cholesterol (mmol/L)		3.6±0.73	4.2±0.99	0.004
Serum total protein(g/L)		73.98±11.1	76.05±6.63	0.290
Serum albumin(g/L)		34.87±6.56	41.00±5.41	0.000
Serum globulin(g/L)		39.11±10.05	35.0±6.51	0.026
24 hr urine protein (g/day)§		2.57±2.42	0.25±0.11	0.000
Serum Creatinine (Ì mol/L)		221.31± 341.42	87.12 ± 42.61	0.003
Creatinine clearance (mls/min)		62.73 ± 38.6	90.98 ± 32.8	0.000
Urine Na+ (mmol/L) *		125.1±42.2	146.27±37.3	0.040
Urine K+ (mmol/L) *		70.41±27.9	68.81±15.26	0.78

The histopathology in a few showed essentially focal glomerulosclerosis with microcystic tubular dilatation, mononuclear cell proliferation and interestial fibrosis. The high prevalence of renal disease in HIV – a continuing largely uncontrollable scourge – and the high risk for ESRD, will certainly stretch the limited facilities for renal replacement therapy in Nigeria[26]. More rigorous community studies of the prevalence and risk factors for the development of ESRD will inform appropriate preventive strategies.

At present only 2 centres provide dialysis support for patients with renal failure associated with HIV infection. There is a need to open up renal replacement facilities for the increasing number of patients, through appropriate legislation based on equity and relevant education of healthcare providers.

More rigorous community studies of the prevalence and risk factors for the development of ESRD will inform appropriate preventive strategies.

P.Malariae induced Glomerulonephritis: (Quartan Malarial Nephropathy,Tropical nephropathy)

This entity was described in Nigeria by Hendrickse et al (1972)[27], and other researchers in the tropics (Habib 1973[28], Kibukamusoke, 1971[29], Morel Maroger et al, 1975[30]). The evidence in support of causal relationship between P. Malariae and the nephritic syndrome was based on epidemiologic, experimental and clinico-pathological observations by various researchers. The epidemiological evidence derives largely from the observation of Giglioli (1962b)[31] who pointed out the virtual disappearance of the nephritic syndrome in Guiana after the eradication of malaria. This view was supported by Hendrickse[27] who found a highly significant increase in P. malariae parasitaemia in the nephritic children. It has however been argued that this may be due to an increased susceptibility of the nephritic child to P. malariae infection.

The experimental evidence is based on the work of Voller et al (1973)[32] who described nephritic syndrome in one splenectomised monkey about 20 weeks after infection with P. malariae.

Perhaps the backbone of the body of data establishing the casual relationship between P.malariae and the nephritic syndrome is the similarity of glomerular histology in cases of nephritic syndrome associated with P. malariae parasitaemia, and also those largely encountered in the P. malariae endemic regions (Hendrickse et al 1972)[27]. This has been further corroborated by the demonstration of P. malariae antigen along the glomerular basement membrane in up to 30 percent of cases[27]. The

possibility of P. malariae triggering off other immunopathogenetic mechanism like Deoxyribonucleic acid (DNA) anti DNA immune complexes has been entertained in cases where P. malariae antigen could not be demonstrated.

P. malariae nephropathy is characterized by a progressive segmental and focal glomerulosclerosis. The basic lesion is a thickening of the capillary wall which in the earliest cases affects only few glomeruli in a segmental fashion. This thickening involves the subendothelial aspect of the basement memberane, giving rise to a double contour of periodic acid Schiff (PAS) – positive, argyrophilic fibrils. There is messangial expansion with immune complex deposits mostly IgCa and C3.

Benefits from prednisolone or immunosuppressive drugs have been reported in a few children especially those with highly sensitive proteinuria, mild histologic lesions and short duration of symptoms. (Adeniyi et al 1970[33]).

Figure 12: Showing Quartan Malarial Nephropathy. P malariae GN: PAS stainning of the glomerulus showing focal segmental sclerosis (in an 8-year old child).

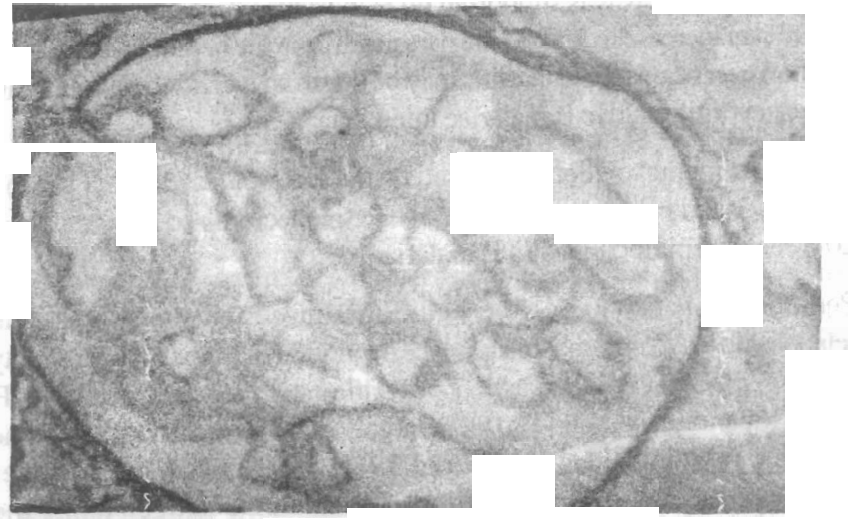
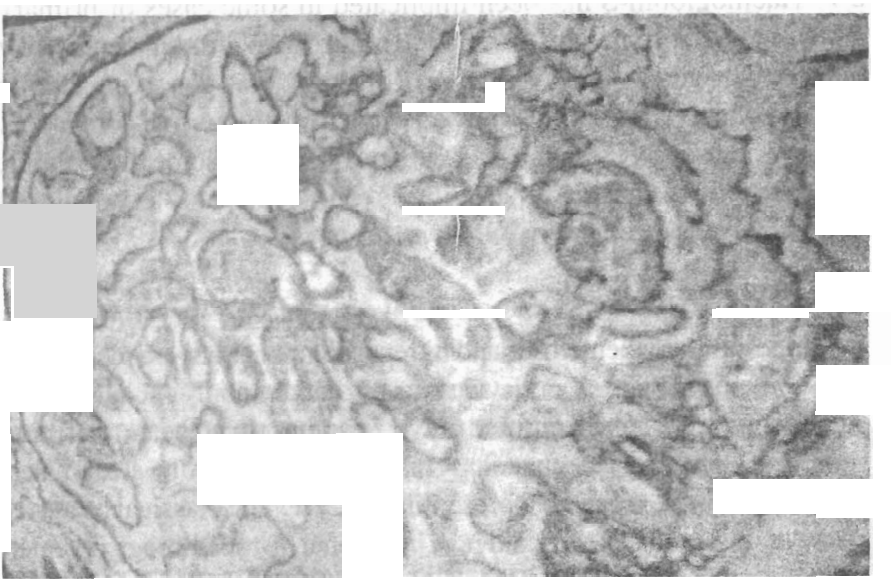


Figure 13: P malariae GN with glomerulus showing non uniform thickening of the gl. capillary wall with splitting in places, sparse mesangial cellularity & matricial expansion (Masson Trichome stain).



Our effort to implicate P. malariae in adult glomerulonephritis and chronic kidney disease has been relentless. The prevalence and density of malarial parasitnema in adult nephrotic syndrome and chronic kidney disease is not significantly different from controls. Even though the renal histological pattern of focal segmental Glomerulosclerosis and mesangiocapillary GN seen commonly in adult GN appears similar to those reported in childhood P. malariae nephropathy, it is conceivable that it is a reflection of the limited responses of the kidney to injury – whatever the injury – and not specific to P. malariae infection. We have however occasionally encountred cases of older children with the classical histological finding of P. malariae nephropathy [Figure 12 & 13]. It is however possible that this may be a reflection of the limited response of the kidney to injury rather than a specific to malaria.

Haemoglobin-S disease and GN

The prevalence of HB-S is 25% in the Nigerian population, and it occurs predominantly in the heterozygous state AS, and less frequently as SC or SS. Haemoglobin-S has been implicated in some cases of primary glomerulonephritis but this association is infrequent in adult nephrology practice in Nigeria. The distribution of Haemoglobin genotypes among the GN patients is not significantly different from the normal population. We have occasionally seen some SC or SS patients with glomerulonephritis, complicated by chronic renal failure. The commonly encountered histopathology is proliferative GN.

SLE Nephritis

Systemic lupus erythematosus and its renal complications are recognized to be common in blacks world wide but very uncommonly encountered in our practice[34]. We have identified only 12 patients (in 10 years) fulfilling American College of Rheumatology diagnostic criteria. All were females, age range 15 – 52 yrs, with 7 presenting in CRF. The classical butterfly rash was observed in 2, Discoid rash in 2. Renal histopathology revealed Diffuse Proliferative GN in 3; MCGN 1 and Minimal Change in 1.

Hypertensive Nephrosclerosis:

The etiological role of hypertension for renal disease in the clinical entity called Hypertensive nephrosclerosis is not in doubt, while its major contribution to ESRD particularly in blacks has been widely reported. In a land mark 16 year prospective study of 361,662 men, aged 35-57 years who participated in the multiple risk factor interventional trial, it was observed that

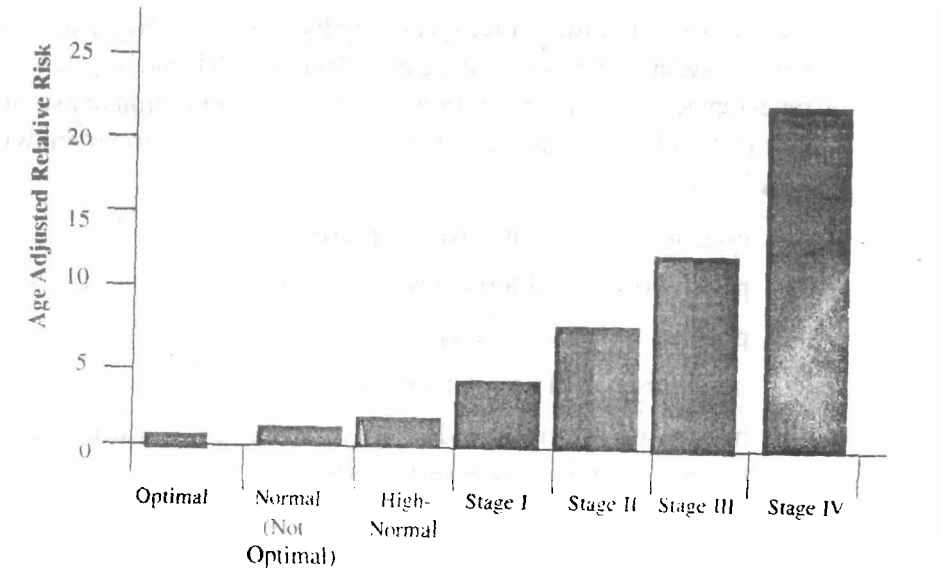
(i) 814 died of renal failure/ESRD (49% due to hypertension).

(ii) age adjusted rate of ESRD per 100,000 persons was 205.6 compared to 5.3 in individuals with SPB≥180, DPB 110 mmHg and SBP of <120/80 respectively

(iii) absolute risk of ESRD was highest for those with a baseline BP in the highest category of SBP and DBP, and

(iv) the relationship of BP and renal damage was positive and continuous through the blood pressure range. In another study of 11912 males followed up for 13.9 years in the Veterans Admin hypertensive screening and treatment regimen, baseline BP predicted ESRD and 15 years later (Table 13)[37].

Figure 14: End stage renal disease and blood pressure



Culled from Klag et al[37]

Hypertensive nephrosclerosis accounts for between 25-50% of the causes of CFR (our reports and others) in Africa, 22 - 40% in the USA and 8% in Europe[1,35-43]. It has been speculated that a number of factors acting in concert with hypertension promote the development of hypertension related CRF. These include age, black race, severity of hypertension; socio-economic factors, availability and utilization of hospital facilities, compliance with therapy and type of drugs; body mass index; social habits; alcohol intake; and cigarette smoking; high salt intake and concomitant systemic disease. Dyslipidaemia, oligonephronia, preterm birth. It is thus probable that the increased prevalence of hypertension induced CRF among the black Americans may be due to a preponderance of these factors.

An active control of these factors among hypertensive Nigerians will certainly translate to reduction in the prevalence of CRF and huge savings on renal replacement therapy. Observations from our preliminary studies on risk factors for hypertensive nephrosclerosis are in agreement with others elsewhere that

- higher blood pressure levels at presentation.
- poorly controlled blood pressure levels.
- poor compliance to therapy.
- non-utilisation of hospital services.
- higher body mass index, persistent microalbuminuria, hyperglycaemia constitute risk factors.

We have further evaluated the implications of microalbuminuria among uncomplicated hypertensives[44]. It was observed that

- microalbuminuria was present in varying levels in 70% of patients.
- Levels correlated significantly with the presence of other target organ damage – left ventricular hypertrophy by ECG; left ventricular mass index (ECHO); retinopathy and also glomerular filtration rate.

Therapy targeted at aborting microalbuminuria in the uncomplicated hypertensives should prevent development or evolution to hypertensive nephrosclerosis and CRF.

The institution of this strategy presupposes the identification of microalbuminuria as a marker for onset of nephrosclerosis. Effective strategies should therefore include early detection and goal – focused treatment of hypertension with drugs that do not only reduce blood pressure but protect the kidney by reducing glomerular hypertension, abort microalbuminuria notably ACE inhibitors and calcium channel blockers) [45]. Longitudinal studies of risk factors for hypertensive nephrosclerosis have to be undertaken on a national scale.

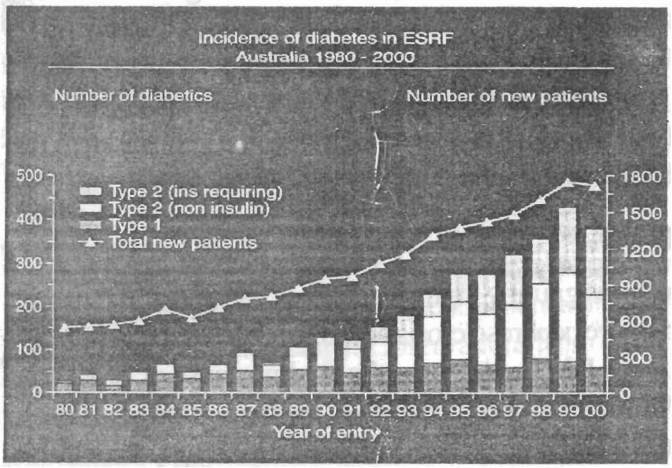
Diabetic Nephropathy:

Diabetic Nephropathy is gaining significance as a cause of CRF and it may displace hypertensive nephrosclerosis or CGN as it has done in Europe and in USA[46,47]. Indeed DM has become the leading cause of ESRD in many countries of Western Europe. In the USA, the proportion of patients with DM as the cause of ESRF (incidence) increased strikingly from 27% in 1988 to 36% in 1992 and 40% in 1995[48,49]. It has also been reported that a continuous increase in the number of patients with type 2 DM admitted for RRT has also recently been noted in Europe and Australia (Figure 15). Diabetic Nephropathy is now one of the leading causes of ESRD (exceeding 30-40%) in countries such as Malaysia. Turkey, Qatar and the Phillipines. [49].

In all European Countries even in those with a relatively low prevalence of diabetic nephropathy. the number of patients with type 2 DM admitted for renal replacement therapy has recently increased. A high prevalence of DN with ESRD has been observed among Afro Carribeans and Asian individuals in the UK[50]. Survival and medical rehabilitation of patients with type 2 DM on renal replacement therapy is significantly worse than in non-DM

patients. It is obvious that in other to stem the tide, intensive efforts are necessary.

Figure 15: Incidence of Diabetes in ESRF Australia 1980-2000



Culled from Ritz et al [47]

to inform the medical community about the renal risk of type 2 DM and the striking effectiveness of preventive measures.

(i) to provide better care for diabetic patients and DN-through-antihypertensive treatment with ACE inhibitors, intensified glycaemic control, cessation of smoking, reduction of protein intake, use of lipid lowering drugs and

(ii) to reduce the high prevalence of the western life style

all in an effort to mitigate factors that promote the progression of renal damage in diabetic nephropathy viz:

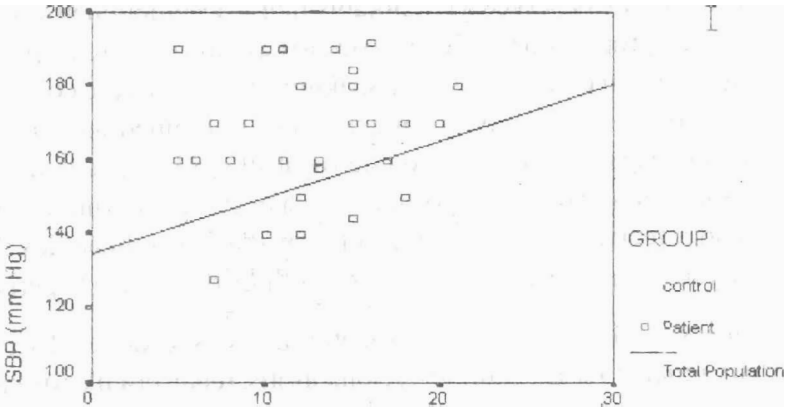
- Systemic hypertension
- Microalbuminuria
- Proteinuria

  Hyperglycaemia
- Activation of the rennin-angiiotensin system

  Smoking

In our published works (Arije, Akinsola & Ladipo[51], Ikem & Akinsola & others[52], Ibrahim, Akinsola et al[53]) we noted that hypertension, poor glycaemic control and long duration of diabetes were potent risk factors for the development of diabetic nephropathy, while smoking, BMI and hypercholesterolemia surprisingly did not distinguish between DN and DM without nephropathy. A preventive strategy should be built around detection and adequate treatment of hypertension, glycaemic control and longitudinal follow up.

Figure 16: The relationship between SBP and duration of DM r=0.284, p=0.025.



DRUGS:

Various drugs ranging from analgesics such as acetaminophen, nonsteroidal antiflammatory drugs; antibiotics to a variety of others have been incriminated in renal failure .In traditional societies like Nigeria, drugs are taken in the form of herbal preparations .Some of the herbal preparations contain unknown agents: biological, plant and chemical toxins such as Mercury(Hg) and Cupper that may be nephroxic. Although the exact magnitude of this problem is not known, our studies as well as others have identified some patients who present in an acute renal failure setting, but with poor prognosis. In a significant proportion of patients, herbal therapy may also precipitate acute on chronic renal failure[54,55]. The inventory of the various herbal preparations is required for a proper understanding of their role in CRF and this calls for collaborative studies between nephrologists/toxicologist/traditional medical practitioners and the drug monitoring agency.

Analgesic nephropathy is recognized as a common cause of CRF in Australia and some European countries, and it occurs more commonly among females who have consumed at least 1.0 kg of analgesic mixtures[56]. In our study – an epidemiological survey of analgesic consumption among labour workers, we observed a remarkably high consumption in a small but significant proportion who also tended to have a higher frequency of symptoms of renal disease[57]. A very striking finding was the common practice among many people of ingestion of combined analgesics-paracetamol, phenacetin, codein, non steroidal anti-inflammatory drugs-what is named "power drug"—a potentially kidney damaging 'innovation'. Proper and effective drug education at the primary healthcare level is mandatory to stem the pervasive practice of self medication in Nigeria

Other causes of CRF – obstructive uropathy, polycystic kidney disease, hereditary renal diseases, chronic pyelonephritis, renal vascular disease are infrequently encountered.

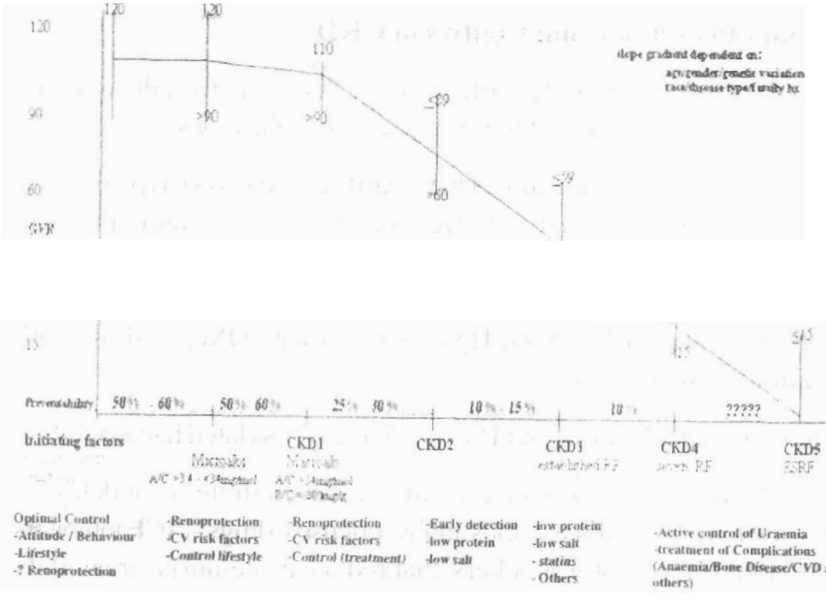
•

MANAGEMENT:

The management of chronic renal failure is one of a continuum- commencing from prevention of the development of the disease in people at risk and the general population, to retarding of the progression in those in whom it has developed, and to prevention of complications of the disease, and mitigation of the effects of the disease.

A coordinated community, clinic and hospital based programme with the active engagement of everybody in the community and the government is advocated. A graph showing the point of intervention from that of promotion of renal health, through health education on the right attitudes/ behavioral practices to full replacement of renal function is provided below (Figure 17).

Figure 17: Progression of Chronic Kidney Disease and Interventional Strategies.



The Management of chronic kidney diseases can be done at 3 levels of care: (i) **Primary healthcare level** – mainly targeted at the prevention of the development of renal disease in those at risk and could be a community approach or at selected clinic populations; and the promotion of renal health through appropriate health education on the right attitudes, behavior and practices that may promote renal health[58]. These include healthy living i.e. avoidance of smoking and excessive alcohol, regular exercise, optimal body weight, balanced diet – (with moderate salt, low saturated fats, rich in fruits and vegetables); avoidance of self medications, and indiscriminate use of analgesics and herbal medications and skin lightening creams, restricted exposure to environmental pollutants like heavy metals and hydrocarbons; and improved health seeking attitude. Individuals with specific conditions such as Hypertension, Diabetes Mellitus, family history of renal disease, recurrent urinary tract infection and obstruction and other risk factors should be screened regularly. Treatment should include use of renoprotective drugs particularly in patients with hypertension, DM and glomerulonephiritides.

Secondary Prevention and Control of CKD:

The goals are (i) early detection of renal disease, (ii) halting of its progression, (iii) mitigation of the effects and complications.

Treatment of the underlying cause of the renal disease if known is particularly rewarding, as it will retard the progression of the disease particularly in cases of hypertension and Diabetes. Target blood pressure levels in patients with CKD should be less than 130/80 mmHg in the absence of diabetes or proteinuria and <125/75 mmHg in patients with DM and those with proteinuria in excess of 1g/24h.

Target blood sugar levels should be 6.5 -7%, glycosylated haemoglobin.

Control of albuminuria/proteinuria is also a proven strategy for delaying the progression of renal disease, thus antihypertensive drugs – ACE inhibitors and Angiotensin receptor blockers that reduce proteinuria, are widely advocated[59]. They may also have additional renoprotective effect through

inhibition of renal inflammation and fibrosis. Lipid lowering has been suggested to ameliorate CKD thus favouring the use of statins in addition to antiproteinuric drugs. In addition, diet and life style modifications – such as weight reduction, regular exercise and dietary regiment of salt restriction and diets rich in fruit and vegetables and low in saturated fat should be adopted.

In the glomerulonephritides, modulation of the immunopathogenic process can be effected with the use of anti-inflammatory and immunosuppressive drugs.

Dietary Management:

Dietary manipulation is very effective in early and moderately severe cases (serum creatinine levels < 500μmol/1). It stabilizes renal function. In a collaborative study with nutritionists we constructed a dietary regimen, based on the available local staples (Table 14) – providing protein (20 – 30 g per day), of high biological value made up of fish, egg protein and or cray fish; and high calorie intake (3000 kcal/day) derived from locally available food items – cassava, yam, corn e.t.c; and low sodium (60 mmol) and potassium (40 – 60 mmol).

Table 14: Sample day's menu providing 25-30g protein, 3000kcal, 60 mEq (1380mg) Na^+, 40-60mEq (1560-2340 mg) K^+

	Protein (g)	Na^+ (mEq)	K^+ (mg)	kcal
Breakfast				
Moderately thick pap	-	-	950.0	164.0
One (20k worth) salt free akara ball (approx. 50g)	4.36	Neg	87.1	199.0
Lunch				
Eba (2 ½ Kitchen spoon scoop = approx. 400g	1.73	10.0	710.0	573.6
Okro (5 large. approx. 50g)	0.9	1.5	142.5	15.5
Stew (small onion/tomato/ twokitchen spoon scoop oil)	Neg	Neg	72.9	720.0
One 50k worth piece of meat or fish (30g)	7.6	16.8	111.0	86.5
Supper				
Three heaped kitchen spoons plain boiled rice (approx. 300g)	5.28	15.0	225.0	550.0
Stew (small onion/tomato/ two kitchen spoon scoop oil)	Neg.	Neg.	72.9	720.0
One 50k worth piece of meat or fish (30g)	7.6	16.8	111.0	86.5
Total	27.47	59.8	2482.4	3115.0

Akinsola et al[60].

*At today's naira value: 1k = 0.5N; 10k = N5.00

Seven patients (5 males, 2 females) with mild to moderately severe CRF were followed up on this regimen for a period ranging from 9 to 28 months. Protein intake was assessed by 2-day dietary recall. The rate of progression of renal failure was significantly lower in the study cases than

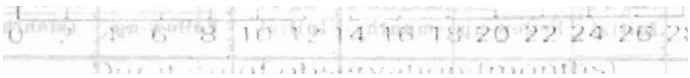
the controls. There was improvement of clinical symptoms of uraemia, and stability and improvement of renal function [Table 15: Figure 18][80].

We further introduced a-keto-analogues of Amino acids available in form of – Ketosteril tablets – to supplement the low protein intake in a few patients that could afford the therapy. We observed a significant improvement in quality of life and respite from uraemic symptoms. In Nigeria high quality protein is very expensive and ketoanalogues are outrageously so. Compliance to the dietary therapy is further worsened by the monotonous and unpalatable nature of the regimen. Culture, customs and tradition are also strong barriers to dietary therapy. There is a need to examine all these constraints while packaging an acceptable food table from our local staples, for the treatment of CRF.

Table 15: Table of patients and parameters

Patient No.	Study group			Controls		
	Serum (mg%) Initial	creatinine Follow-up	Duration observation (months)	Serum (mg%) Initial	creatinine Follow-up	Duration of observation (months)
1	5.0	5.8	16	4.1	5.3	9
2	7.3	6.7	24	4.1	5.8	16
3	4.5	4.2	22	4.8	7.8	16
4	5.0	6.6	28	3.0	7.3	18
5	2.3	2.2	16	5.9	6.3	16
6	2.4	2.3	28			
7	2.7	2.7	18			

Figure 18: Relationship of the reciprocal of serum creatinine concentration plotted against time in the study group (a) and control group (b). (a) n=7, slope =-0.00092; duration of observation = 18-28 months. (b) n=5, slope =-0.0056; duration of observation = 9-18 months.



Akinsola et al[60].

Tertiary Management:

The goals are to mitigate the effects and complications of renal failure and replace renal function by dialysis or renal transplantation:

Haemodialysis

Dialysis intervention as a maintenance therapy in ESRF (creatinine ...5ml/min) has been successful and its practice continues to improve with development of biocompatible, high flux dialysis membranes, high precision, high-tech, computerized dialysis machines and effective control of anaemia with erythropoietin and effective control of renal osteodystrophy and improved patient education. The costs of these management strategies

are enormous and even in the developed economy with good infrastructure, are a cause for concern. Maintenance haemodialysis is largely not feasible in Nigeria due to

- High cost of machine maintenance services,
- Lack of trained personnel and
- The high prevalence of heapatitis B and indeed
- The emerging scourge of HIV,
- Incessant work disruption occasioned by industrial disputes and
- Poorly developed infrastructure,
- unsteady supply of treated water and electricity;
- poor road and communication network.

We have observed that high cost of dialysis and distance of patients' homes to centre are major constraints to effective dialysis as the dialysis facilities are available only in major city centres. At a cost of between US$70 – 100 per HD session and US$1500 3000 per month (against per capital income of US$400) for the dialysis service and laboratory investigations and drugs, only a tiny fraction of our patients can afford this treatment. In our survey of renal centres, we found that majority of the patients – proportions varying from 38 – 90% could afford only one HD session, while between 30 – 40% could afford 2 sessions and percentages varying from 0 – 90% could not afford even one HD session[3,6].

To promote maintenance dialysis as a management option, there will be need for government subsidy and local sourcing of dialysis hardware and consumables. This needs a bold initiative from our government. Majority of Nigerians live in the rural area with poorly developed infrastructure and where they have access to only primary and secondary health care facilities.

Maintenance dialysis therapy in the form of continuous ambulatory peritoneal dialysis (CAPD) should overcome most of the constraints associated with maintenance HD. It is practicable in the rural communities.

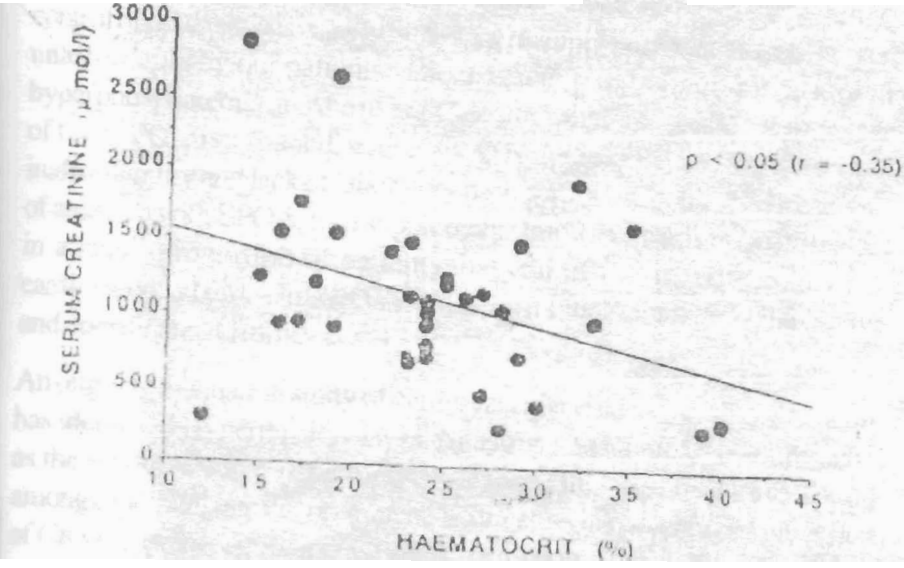
Continuous Ambulatory Peritoneal Dialysis – Practicability and Prospects:

Experience with CAPD is very limited in Nigeria inspite of its practicability, prospects and suitability particularly in a resource poor and low technology environment as ours. Our published experience stands out as providing the guiding lights into this modality of renal replacement in this country. We studied 8 patients who were offered CAPD for periods ranging from 2 weeks to 9 months with a total of 39 patient-months showed the feasibility and practicability and the benefits of this treatment[62]. There was a good blood pressure control, while the requirement for blood transfusion was minimized. 4 of the patients returned to work as quality of life and good rehabilitation were achieved. Complications encountered included, peritonitis occurring in 87.5% with 14 episodes during a total of 39 months of treatment. *Staphylococci epidermidis, Pseudomonas* and unspecified *coliform* organisms were isolated from culture. Other complications were sepsis syndrome in 2, hypoalbuminaemia in 3, pain on running in fluid 2, rupture of line 1, bloody effluent 2, hyperlipidaemia in 2, pleural effusion 1, hyperglycaemia and pancreatitis in 1.CAPD seems an attractive option of management in the rural communities. Availability of fluids and software and consumables could be inproved with local sourcing of these. Peritonitis – a major constraint should be tackled with improved technique, patient selection, adequate patient training and adequate / optimal dose of dialysis (through assessment using relevant methods – kinetic modeling/ protein catabolic rate e.t.c. Only physicians with training and experience in this technique should supervise CAPD programmes. Institution of a national CAPD programme provides an opportunity for the rural communities to benefit from one form of renal replacement therapy which is not available to that large proportion of Nigerians. Sadly our efforts through informal/informal interactions with successive governments and indeed those whose slogan was "Better Life For Rural Women" have been unrewarding. There is a need for legislation on minimum health standards for every Nigerian, rural or urban in the spirit of equity.

ANAEMIA and EPO treatment:

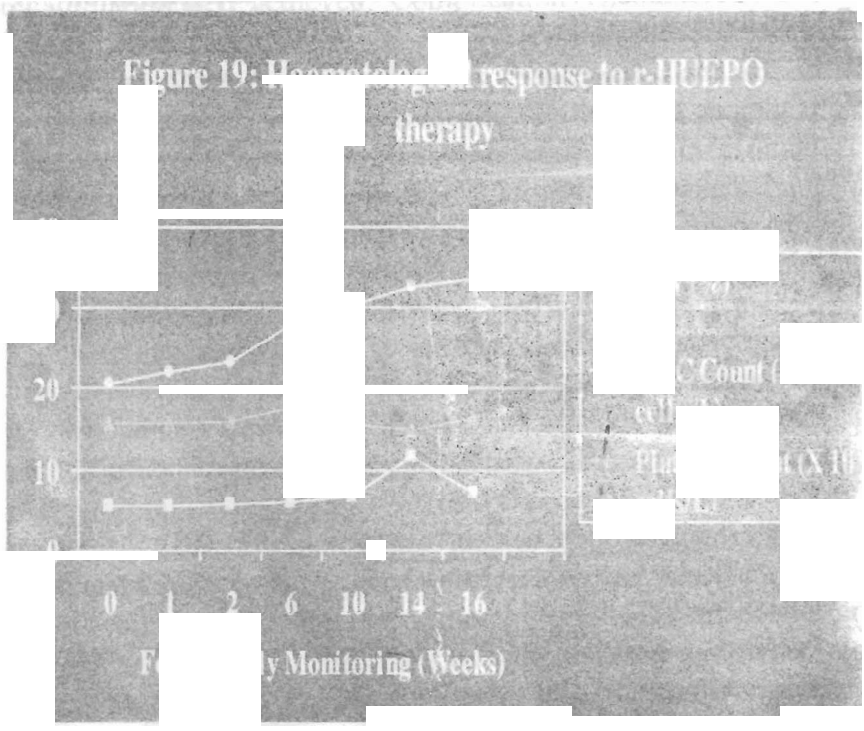
Anaemia is common in patients with chronic renal future and is associated with significant morbidity and mortality. Severe anaemia (below 18%) was found in about 25% of the patients in our study[63]. Many factors have been incriminated in its etiology, namely bone marrow hypoplasia, increased red cell destruction, increased tendency to bleed, while reduced erythropoietin production and uraemic toxins have been considered fundamentally responsible. A significant inverse relationship was observed in many studies (including ours[63]) [Figure 17] indicating that the severity of renal failure is an important factor in the level of the anaemia.

Figure 17: Relationship between serum creatinine concentration (umol/L) and haematocrit (%).



Akinsola et al[63]

We have noted in another study a prominent role of Iron in a significant proportion of patients, who demonstrated reduced stainable bone marrow Iron and low Transferin saturation and who responded dramatically to parenteral Iron[64]. That finding is of practical importance in a resource constrained environment as ours as it would significantly reduce the use of Erythropoietin which is not affordable by most of our patients. Our experience with Erythropoietin has been reported and it is in agreement with the observed beneficial effects of this therapy in patients who are well dialysed and have good iron status (Figure 19)[65]. Treatment with iron and recombinant erythropoietin (EPO) is generally very expensive everywhere and it is available at subsidized rates to make affordable. Generic EPO should be made available at affordable cost to our patients.



CARDIOVASCULAR MORBIDITY AND MORTALITY:

In recent times, excess cardiovascular morbidity/mortality has been associated with CKD even in the early stages before patients develop end stage renal failure. CKD is regarded as a most potent cardiovascular risk factor by itself.

A number of cardiovascular events including congestive cardiac failure, cardiac arrythmias, cardiac ischaemia/infarction, strokes and peripheral vascular diseases are seen in renal failure. The associated risk factors include Hypertension, LVH, Anaemia, dyslipidaemia, obesity, cigarette smoking, insulin resistance, Calcium/Vit. D/Parathromune disturbances, C-reactive protein and a number of others. The burden of the cardiovascular disease events in patients with CKD /CRF is ill-defined, thus efforts at preventing or controlling them will remain conjectural.

At present, control of hypertension is with an antihypertensive regimen which includes ACE inhibitors and this is not effective in many cases; control of lipidaemia is usually by dietary manipulation as statins are largely unaffordable by our patients. Dietary manipulation for the control of hyperphosphatemia and the use of Calcium supplements are the mainstay of Ca & PO_4 disturbance, while Vit. D is generally not given due to its inaffordability and lack of laboratory monitoring facilities. The treatment of anaemia with EPO & Iron supplements improves cardiovascular status in a small proportion of patients that can afford it. The control of cardiovascular burden in CKD should be by multidisciplinary, collaborative and coordinated efforts.

An ongoing evaluation study of cardiovascular risk factors in our patients has identified Hypertension, LVH, Anaemia and Diabetes Nephropathy as the predominant risk factors, while those that are commonly found among caucasians are not prominent[6]. Strategies at preventing progression of CKD must incorporate these risk factors in their design.

Renal Transplantation:

Renal transplantation (RTx) is globally adjudged the best modality of renal replacement therapy in view of its cost-effectiveness and efficiency and a near return to normal life by the patient and it should be preferred even in a resource – constrained economy as ours. It is however complex and elaborate in organization. This form of therapy was unavailable in Nigeria or West Africa subregion, until our hospital and a private hospital pioneered it, with ours being distinctly wholly indigenous. Surgical and medical management was entirely by our local staff. That feat justified the status of our hospital as a designated centre of excellence in renal medicine. Even though that development marked a major 'triumph' in renal care medicine in Nigeria, it nevertheless opened up new challenges and trials. The daunting challenges have been highlighted in our initial report of the first 3 cases[67]. Maintenance /life-long immunosuppressive therapy is the mainstay of transplantation, but no sooner we transplanted than our patients ran out of drugs, as financial support from the enthusiastic philanthropists petered out.. This leads to repeated episodes of acute rejection and subsequent loss of graft. Immunosuppressive drug monitoring facilities are not available and this continually tasked our clinical judgement. Diagnostic facilities for sepsis – particularly viral are inadequate as are potent specific antiviral drugs. A centralized tissue typing facility and well trained and committed renal medical and surgical staff are required. Adequate investigative facilities (laboratory and radiology) and nutritional and counseling unit are a priority. Perhaps the greatest rate limiting factor is availability of donor organ.

Organ procurement is a major constraint and is influenced by the attitude, behaviour and practice of the people all which are intricately tied to the culture, customs and tradition of the people. We have in one epidemiological study evaluated the attitude, behaviour and practice of Nigerians to organ donation. We compared these between hospital workers, relatives of potential transplant patients (patients with ESRF) and healthy rural dwellers. We were impressed by the positive attitude to organ donation inspite of the widely held belief in reincarnation. This attitude

was expressly not motivated by any reward or monetary benefits[68]. This kind of study is very crucial to the establishment of RTx program in this country. RTx is also acceptable to a large majority though some would not agree to transplant, rather preferring to die. That study also revealed that knowledge of renal disease and renal failure is generally inadequate among Nigerians.

Conclusion

Our effort to tackle the problem of CRF should commence with improving our knowledge of renal health. Renal care should therefore be incorporated into primary health care programme and it should include awareness education, screening for hypertension, Diabetes mellitus and proteinuria. Education on risk factors such as unrestricted consumption of analgesic and herbal concoctions as well as exposure to environmental toxins; early detection of chronic renal disease and renal failure by paying attention to features such as nocturia, changes in the frequency of micturition, frothy urine, haematuria, dysuria and loin pains. Efforts at early detection of renal disease will be more rewarding when carried out in childhood.

CKD has assumed a priority public health issue, and it is devastating. There is a need for a national policy to provide a coordinated renal care and set obligatory minimal standard of renal care to every Nigerian citizen, and to facilitate access to life saving/ life preserving procedure such as dialysis or transplantation for the rich or the poor, the city or rural dwellers, the farmer, student, academic, senior government officials, or politician, male or female and young or old. This is the task for all of us!

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