END STAGE RENAL DISEASE: RACIAL DIFFERENCES

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SUMMARY

Objectives: The prevalence and aetiological of end stage renal disease (ESRD) differ from race to race and from location to location even among people of the same race. There is paucity of data on the comparison of ESDR in whites and blacks living in their native environment. The study was undertaken to retrospectively define the differences in manifestation of ESRD in whites and blacks in their natural environment.

Methods: Case records of consecutive patients in chronic renal failure that were seen at the University of Ilorin Teaching Hospital, Ilorin, Nigeria and Guy's Hospital, London, England over a four year (1996 to 1999) and two year periods respectively were reviewed. Data collected included data on sex, age, race, aetiology and usual features of ESRD.

Results: A total of 127 blacks (76 males, 51 females) and 125 Caucasians (74 males, 51 females) were recruited and categorized into groups. The commonest disease causing ESRD in Caucasians was diabetic nephropathy [(DN), 26.4%] followed by chronic glomerulonephritis [(CGN), 16.8%] and hypertensive nephrosclerosis [(HTN), 10.6%]. Amongst blacks, however, CGN (38.6%) was the commonest cause, followed by HTN (26%) and DN (7.05%). In 14% and 9% of blacks and whites respectively, the cause of ESRD was unknown. Most blacks with CGN and HTN reached ESRD in the 2nd and 3rd decades; in any case earlier than whites. DN was thrice commoner in whites with the majority in the 5th and 6th decades in both races.

Conclusion: This study tends to validate the notion that the spectrum of renal diseases in the tropics is generally the same as in the temperate environments, but the prevalence, natural history and major Aetiological factors do vary from race to race and in location. Diabetic nephropathy which was thought to be rare in blacks is becoming a major problem. It is disturbing that a high proportion of blacks reached ESRD within their 2nd to 4th decades when they are still very productive.

Key Words: *ESRD, Race, Prevalence, Aetiology*

INTRODUCTION

Kidney diseases of diverse aetiologies have the potential to culminate in chronic renal failure (CRF). Once CRF is established, it tends to progress to end stage renal disease (ESRD) and measures designed to halt the progression have been largely unsuccessful[1]. The control of some modifiable risk factors such as diabetes mellitus, hypertension, protein intake, disorders of phosphate and calcium metabolism tend to slow down the disease process subject to the type of nephropathy[2]. End stage renal disease marks the point in the disease process where a patient dies if renal replacement therapy is not instituted and maintained.

End stage renal disease is found amongst all races and in all parts of the world, though the prevalence and causative factors may differ from race to race and, even in the same race, in different or same locations. Unlike in Europe and America where the profile of renal diseases leading to ESRD are fairly well characterized, the aetiology of ESRD in Africa is less well known despite spirited efforts made in this direction for the past five decades[3-11]. Studies have shown that Immunoglobulin A nephropathy (IgAN), Diabetic nephropathy (DN) and Chronic pyelonephritis (CPN) are major causes of ESRD among whites while Chronic glomerulonephritis (CGN) and Hypertension (HTN) are the commonest among blacks[3-6,11-14]. The suggested reasons for existing racial differences include genetic, sociocultural factors, inadequate diagnostic tools and therapeutic modalities.

In the developed world, majority of comparative racial studies on ESRD focused on blacks, whites and Hispanics living within the same environment[8-10,14-16]. There is paucity of data on the comparison of the prevalence of ESRD in whites and blacks studied in their native

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environment. We therefore attempt to compare the prevalence and aetiology of ESRD among blacks and whites studied in their natural environment in order to clearly define the differences.

Subjects and Methods

We did a retrospective comparative analysis of race, age, sex and causes of end stage renal disease among black and white patients resident in their native environment using the opportunity of one of us (AC), visiting Guy's Hospital, London for six months on a sponsored fellowship programme in the year 2000. The study was based on consecutive ESRD patients managed at Guy's Hospital, London and University of Ilorin Teaching Hospital, Ilorin Nigeria over the two year period (1998 – 1999 both dates inclusive) and the four year period (1996 – 1999 both dates inclusive) respectively.

The diseases causing ESRD in the two populations were extracted from the patients' case records and categorized into groups: Chronic glomerulonephritis (CGN), Hypertensive nephrosclerosis (HTN), Diabetic nephropathy (DN), Chronic pyelonephritis (CPN), Obstructive uropathy (OU), Adult polycystic kidney disease (APKD), Connective tissue disease (CTD), Myeloma kidneys (MK) and others.

The criteria for the diagnosis of ESRD included most of the following: history of renal disease of more than 6 months duration, uraemic symptoms, azotaemia, shrunken kidneys and or complete loss of corticomedullary differentiation, glomerular filtration rate of less than 5mls/min, dependence on renal replacement therapy (RRT) and or death from uraemia. The diagnosis of causative factors was derived from documented clinical features and results of relevant investigative procedures which included: urine analysis, blood biochemistry, urinary system imaging and renal tissue histology. Chronic glomerulonephritis was diagnosed in the presence of six month history of renal disease, biochemical evidence of nephrotic syndrome, past medical history of profuse proteinuria noted biochemically or recognized by the patients as frothy urine and or histological evidence of glomerular disease defined by examination of either biopsy or autopsy specimen.

Hypertensive nephrosclerosis was diagnosed in the setting that included the following: history of hypertension greater than 1 year, diastolic blood pressure usually above 110mmHg, presence of grade III retinopathy, features of left ventricular hypertrophy and aortic unfolding, presence of microscopic haematuria and moderate proteinuria or renal histologic changes. The features that were relevant in the diagnosis of chronic pyelonephritis included three or more episodes of recurrent urinary tract infections with or without laboratory evidence of pyuria, positive urine culture, ultrasonic and intravenous urographic changes.

The diagnosis of diabetic nephropathy was mainly based on history of diabetes mellitus of more than seven years duration, proteinuria of over 0.5gm/day, presence of systemic hypertension and diabetic retinopathy. The other causes such as obstructive uropathy, adult polycystic kidney disease, connective tissue disease, myeloma kidneys, gouty nephropathy, Alport's syndrome and HIV-associated nephropathy were derived from the relevant clinical features and investigative findings.

Patients in whom a definite aetiological factor could not be implicated from the records were classified as unknown.

All the analyses were by simple proportions and percentages.

Results

A total of 125 Caucasians (74 males and 51 females) and 127 blacks (76 males and 51 females) were reviewed and categorized over a two year and four year periods respectively (table 1). The commonest disease causing ESRD in Caucasians was diabetic nephropathy (26.4%) while the commonest cause in blacks was chronic glomerulonephritis (38.6%).

Table 1
Age and Sex Distribution

Age (Years)	Male		Female		Total	
	Blacks	Whites	Blacks	Whites	Blacks	Whites
10 – 19	5		5		10	
20 – 29	19	3	14	4	33	7
30 – 39	18	7	17	6	35	13
40 – 49	14	7	4	11	18	18
50 – 59	10	13	8	15	18	28
60 – 69	7	27	3	13	10	40
70 – 79	2	15		2	2	17
80 – 89	1	2			1	2
Total	76	74	51	51	127	125

Male: Female ratio – Blacks = 1.5: 1
Whites = 1.4: 1

As shown in table 2, the uncommon conditions such as lupus nephropathy and myeloma kidneys were more common in whites than in blacks while rare entities such as gouty nephropathy Alport's syndrome and cystinosis were not seen in blacks.

Table 2
Aetiology of ESRD

Cause	Male		Female		Total		% of Total	
	Black	White	Black	White	Black	White	Black	White
CGN	25	11	24	10	49	21	38.58	16.8
Hypertension	24	10	9	3	33	13	25.98	10.4
Diabetic Nephropathy	6	20	3	13	9	33	7.08	26.4
Obstructive Uropathy	6	6			6	6	4.72	4.8
CPN	2	1	3	8	5	9	3.94	7.2
CIN		6		2		8		6.4
APKD	2	7	1	1	3	8	2.36	6.4
HIVAN	3				3		2.36	
Lupus Nephritis		3	2	1	2	4	1.57	3.2
Myeloma	1	2	1		2	2	1.57	1.6
Gouty Nephropathy		3		1		4		3.2
Alport's Syndrome		1		2		3		2.4
Cystinosis		1				1		0.8
Unknown	10	3	8	8	18	11	14.17	8.8

CGN: Chronic Glomerulonephritis
CPN: Chronic Pyelonephritis
CIN: Chronic Interstitial Nephritis
APKD: Adult Polycystic Kidney Disease
HIVAN: HIV Associated Nephropathy

Table 3 presents the age/sex distribution of patients who had chronic glomerulonephritis, with majority of affected blacks (83%) being below 40 years of age in contrast with whites 60% of whom were in their 5th and 6th decades.

Table 3
Age and Sex Distribution of patients with CGN

Age (Years)	Male		Female		Total		% of Total	
	Blacks	Whites	Blacks	Whites	Blacks	Whites	Blacks	Whites
10 – 19	3		7		10		20.4	
20 – 29	10	2	5	1	15	3	30.6	15.0
30 – 39	9	4	7	1	16	5	32.6	25.0
40 – 49	2			3	2	3	4.1	15.0
50 – 59	3	2		4	3	6	6.12	30.0
60 – 69	3	2		1	3	3	6.12	15.0
Total	30	10	19	10	49	20	100.0	100.0

When diabetic nephropathy was analyzed, table 4, it was noted to be co-dominant in the 5th and 6th decades among blacks and whites, but relatively rare in the 4th decade and below in blacks compared with its 12% prevalence among whites in the 4th decade.

Table 4
Ages and Sex Distribution of Patients with Diabetic Nephropathy

Age (Years)	Male		Female		Total		% of Total	
	Blacks	Whites	Blacks	Whites	Blacks	Whites	Blacks	Whites
40 – 49		2		2		4		12.1
50 – 59	1	5	2	6	3	11	33.3	33.3
60 – 69	3	11	1	3	4	14	44.4	42.4
70 – 79	2	2		2	2	4	22.2	12.1
Total	6	20	3	13	9	33	100.0	100.0

Hypertensive nephrosclerosis (table 5) peaked in the 3rd decade among blacks in contrast with its peaking in the 6th decade among whites.

Table 5
Ages and Sex Distribution of Patients with Hypertensive Nephropathy

Age (Years)	Male		Female		Total		% of Total	
	Blacks	Whites	Blacks	Whites	Blacks	Whites	Blacks	Whites
30 – 39	4		6		10		30.3	
40 – 49	8	3			8	3	24.2	23.07
50 – 59	3	1	6	2	9	3	27.4	23.07
60 – 69	4	3		1	4	4	12.12	30.76
70 – 79	2	3			2	3	6.06	23.07
Total	21	10	12	3	33	13	100.0	100.0

Blacks were observed to be twice at risk of CGN and HTN with a tendency to occur a decade earlier than in whites. This result showed that less than 20% of blacks with ESRD secondary to CGN and HTN were above 30 years and 50 years respectively. Black males were noted to be more prone to ESRD of diverse aetiologies.

Discussion

Chronic renal failure is an important universally accepted cause of morbidity and mortality especially in tropical developing countries where there is paucity of diagnostic and therapeutic facilities[4-11]. It has been shown from studies that the leading causes of ESRD vary from country to country even in the same part of the world[4-8,11-14]. The contributory factors have included race age, sex, level of awareness, prevailing predisposing factors and available diagnostic facilities. Even where facilities are available, it is very difficult to make distinction between CGN, CPN and HTN especially when recurrent urinary tract infection occurred in a setting of chronic glomerulonephritis. The cause of ESRD may be elusive despite detailed clinical and investigative evaluation. The European dialysis and transplant annual review revealed that about 11% of cases were of unknown aetiology[15].

The observation in this study of CGN as a leading cause of ESRD in blacks is in accord with reports from tropical and temperate countries[4-6,9,16]. This comparative study clearly showed that CGN is more two times commoner in blacks than whites. It is also disturbing to note that over 80% of the blacks with CGN were below 40 years of age. The relatively young age at which majority of patients present with ESRD secondary to CGN in the tropical developing countries have been reported by several authors[4,5,11,12,17]. The reason for the foregoing may be linked with a variety of infective agents implicated in the aetiology of CGN which are present in endemic proportions in the tropics. These agents include infected scabies, plasmodium malariae, Schistosomiasis, mycobacterium leprae, filarial worms, toxoplasmosis, viruses and streptococcal organisms[18-25].

The control of these infections and health education against the use of skin lightening creams and or herbal remedies, which are also

prevalent in the tropics, will reduce ESRD in our environment[26]. In contrast with the tropical environment where majority of primary glomerular diseases are post-infectious, the leading cause of primary glomerulonephritis in Europe is IgA nephropathy, which is thought to be an immune complex mediated disease[24,27,28,29,30]. In view of this, the finding in this study that the majority of Caucasians with CGN are middle aged is not surprising as autoimmune disorders are common in middle age with the kidney being a victim of such immunological reactions. The menace of infectious and communicable diseases, which is still the bane of the tropics, has been largely replaced by non-communicable diseases in the temperate regions. The foregoing is informed by the high level of personal and environmental hygiene with efficient infection control measures.

Hypertension as a cause of ESRD was found in this study to be three times commoner in blacks. This is in accord with reports from tropical and temperate countries, which show that much of the excess risk of ESRD in blacks is due to very high rate of renal failure from systemic hypertension[7-13]. It is therefore not surprising to note that hypertensive nephrosclerosis ranked second to CGN as a cause of ESRD since severe hypertensive disease is commoner among the black population[8,11,12,31,32].

The results of studies on ESRD secondary to HTN should generally be interpreted with caution as it is usually very difficult to tell whether hypertension or insidious renal disease was the primary cause of ESRD. The initial pathological process may elude definition as ESRD is the common end point of longstanding essential hypertension, chronic glomerulonephritis or pyelonephritis. One is often satisfied with a presumptive diagnosis of hypertensive nephrosclerosis in a setting of longstanding hypertension, cardiomegaly, left ventricular hypertrophy, aortic unfolding, hypertensive retinopathy, microscopic haematuria and moderate proteinuria without past history of nephrotic syndrome. The definitive diagnosis will require histologic examination of biopsy or autopsy specimen, which may not be justified. This is because of the difficulty in biopsy and histologic interpretation of tissue changes plus increased risk of post biopsy complications. Since the prevalence and severity of essential hypertension is commoner in blacks, early recognition and prompt treatment of hypertensive disease should be an effective means of preventing or reducing ESRD in blacks[9-13].

We found diabetic nephropathy to be three times commoner in Caucasians than in blacks and also the leading cause of secondary glomerulopathy that culminates in ESRD. This is in agreement with reports from America and Europe[7,10,14-16,27,28]. It may be a reflection of the high prevalence of diabetes mellitus among Caucasians, many of whom live long enough to develop long term complications as majority of the subjects in this study were in the 5th and 6th decades of life. The observation that diabetic nephropathy is the third commonest cause of ESRD in Nigerians is noteworthy as previous studies have documented it to be rare[4,5,8,11,24,33]. Diabetic nephropathy is a syndrome characterized by proteinuria of over 0.5gm/day in a patient who has had diabetes mellitus for more than 10 years, which is usually associated with retinopathy, hypertension and typical histologic changes[34]. Majority of studied blacks with diabetic nephropathy were in the 5th and 6th decades of life which suggest an increase in the prevalence of diabetic mellitus with many of them living long enough to develop long term complications. A change from typical black to Caucasian life stye and perceived improvement in the standard of living may have contributed to the increase in ESRD due to diabetic nephropathy. There is a need for early diagnosis of diabetes mellitus, good glycaemic control and regular screening of diabetic patients for diabetic nephropathy in order to reduce progression to ESRD in them.

The rarity of chronic pyelonephritis (3.9%) as a cause of ESRD among blacks in this study is in accord with the findings in other parts of Africa and Asia[9,35-37]. The finding that CPN was more than twice commoner in Caucasians is in agreement with the experience of Pandreigh et al and Burry in Scotland and Brisbane respectively[6,38]. The reasons for the racial differences in CPN were not clear in this study. Other studies have however implicated analgesic abuse, anatomical anomalies of the urinary tract, vesico-ureteric reflux, benign prostatic hypertrophy and urethral strictures as predisposing factors to CPN[7,38,39]. The racial similarity in the prevalence of obstructive uropathy (4% each) and the virtual absence of chronic interstitial nephritis (CIN) among blacks in contrast with 6.4% of

Caucasians in this review suggests that analgesic abuse may be the major predisposing factor in Caucasians. This is because analgesic abuse, anatomical defects and vesico-ureteric have been noted to be rare among the Negroid race and CPN is usually associated with defects in the urinary tract[39]. Most of the blacks with obstructive uropathy in this study had benign prostatic hypertrophy and or urethral stricture, which is in accord with other reports from tropical environemnts[4,5,11,36,40]. There is need for routine screening of adult males for benign prostatic hypertrophy (BPH) and educate the general public on prevention of and adequate treatment of sexually transmitted diseases (STD). These measures will substantially reduce the prevalence of ESRD secondary to obstructive uropathy in the tropics.

Autosomal dominant polycystic kidney disease as a cause of ESRD was found to be three times commoner in Caucasians when compared with blacks. The finding of 6.4% prevalence among Caucasians falls within the range of 6 – 10% observed in North America and Europe[41,42]. The rarity of ESRD due to polycystic kidney disease among blacks in this study is in agreement with other studies in the tropical developing countries[4,5,33,36]. The racial difference in the prevalence of polycystic kidney disease as a cause of ESRD is difficult to explain as the disease is a hereditary disorder. It is possible that many blacks with polycystic kidney disease die earlier from other complications of the disease or that it runs a benign course in blacks. It is also possible that the Caucasian polycystic kidney disease tends to run a more progressive course or that the extra renal complications are better managed thus allowing them live long enough to develop ESRD.

The other rare causes of end stage renal disease such as lupus nephritis, myeloma kidneys, gouty nephropathy and Alport's syndrome did not reveal particular racial predilection except that gouty nephropathy, Alport's syndrome and cystinosis were not seen among the population studied. End stage renal disease of unknown cause as noted in 14% and 9% of blacks and whites respectively is not surprising as proceedings from European Dialysis and Transplant Association showed that about 11% of ESRD were of unknown aetiology. The higher percentage of cases of unknown cause in the black population may be due to paucity of diagnostic facilities and that even when available, it is often beyond the reach of the average Nigerian patient.

The results of this study support the notion that the spectrum of renal diseases in the tropics is generally the same as in temperate regions, but the prevalence, natural history and major aetiological factors may vary from race to race and even in the same race in different individuals whether located in different places or different locations. Diabetic nephropathy still remains the leading cause of ESRD among Caucasians and is three times less common in blacks. It should no longer be considered a rare entity in blacks as it is the 3rd commonest cause of ESRD in this study. The commonest cause of ESRD in blacks was CGN which was closely followed by HTN and both conditions were twice and thrice commoner in blacks in comparison with Caucasians. The disturbingly high percentage of blacks that reached ESRD secondary to CGN and HTN in their 2nd to 4th decades of life is a major cause for concern as they fall within the productive age group. This underscores the need for preventive nephrology especially in the tropics where majority of causative factors are preventable.

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