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The profile of adult nephrology patients admitted to the Renal Unit of the Universitas Tertiary Hospital in Bloemfontein, South Africa from 1997 to 2006

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Abstract

Background. This paper reports a retrospective audit of new patients referred to the Renal Unit at Universitas Academic Hospital in Bloemfontein, South Africa for the decade 1997–2006.

Methods. All the files kept in the Renal Unit were reviewed for the main clinical presentation, a definitive pathological diagnosis (if obtained), age, race and gender of the patients. No consultations from other disciplines were included.

Results. One thousand two hundred and sixteen patients were included in the study. The main clinical presentations were as follows: chronic renal failure (CRF), 461 (37.9%); nephrotic syndrome, 203 (16.7%); hypertension, 161 (13.2%); and abnormal urinary findings, 128 (10.5%). The nephrotic syndrome was the most common indication for renal biopsy, and histological investigation revealed focal segmental glomerulosclerosis in 46 (3.8%) patients, minimal change in 23 (1.9%), membranoproliferative disease in 36 (3.0%) and membranous glomerular disease (MN) in 28 (2.3%). In CRF, hypertension was suspected in 236/461 (51.2%) cases but was proven histologically in only 13 (2.8%) patients.

Conclusions. Socio-political factors impacting on access to healthcare most likely had an influence on the referral pattern of patients during this period. The largest group of patients were referred to our institution late in their disease with CRF, often requiring renal replacement therapy, and a definitive diagnosis was seldom possible at that stage.

With the limited availability of dialysis facilities, the need for early detection and preventative measures with regard to renal disease in this community is evident.

Keywords: disease; kidney; South Africa

Introduction

South Africa has separate private and public healthcare sectors, serving approximately 20 and 80% of the population, respectively [1]. The Free State province is situated in central South Africa with a population of 2,707 million [1]. Its economy is mainly based on agriculture and mining. The only tertiary medical institution serving the public sector in this area is Universitas Academic Hospital in Bloemfontein, the capital of the Free State province. During the previous political dispensation, this hospital was mainly reserved for white patients, but after 1994, racial segregation was abolished in South Africa.

It is suspected that several forms of renal disease in the third world may differ in prevalence, natural course and/or outcome from those in developed countries [2]. Untreated renal disease may cause renal failure that requires renal replacement therapy, which is extremely expensive and places a severe burden on the healthcare budget [2]. This has led to criteria limiting this form of treatment in the South African public sector to only a selected few patients who are transplantable and do not have significant extra-renal disease [3]. These criteria have been criticized [4] and are currently under review.

Previous reviews of renal disease in South Africa revealed that glomerulonephritis and hypertension were reported as the most important causes for end-stage renal failure in early studies with differences noted among racial groups [5]. More recently, the impact of lifestyle and human immunodeficiency virus (HIV) infection is suspected to be more prominent [6]. However, the prevalence of the different forms of renal disease in the Free State is unknown, which leads to arbitrary allocation of manpower and resources. This is a retrospective descriptive audit of all the patients referred to and primarily managed in the Renal Unit at the Universitas Academic Hospital during the period 1997–2006.

Patients and methods

All files stored in the Renal Unit database from January 1997 to 31 December 2006 were reviewed. The following data were captured on a Microsoft Access database:

(1) Age: All patients 13 years and older were included.

(2) Race

(3) The predominant clinical features at presentation were grouped under the main renal syndromes defined as follows:

   (1) abnormal urine sediment: asymptomatic patients with abnormalities on urine examination or proteinuria >0.150 g/day–<3.5 g/day

   (2) nephritic syndrome: patients with haematuria, hypertension and edema

   (3) nephrotic patients: patients with proteinuria >3.5 g/day

   (4) chronic renal failure (CRF): patients with an elevated s-creatinine (>130 μmol/L) and small kidneys on imaging without evidence of reversible causes

   (5) acute renal failure: patients with an elevated creatinine (>130 μmol/L) and normal or large kidneys on imaging with evidence of improvement with therapy

If elements of more than one clinical syndrome were present, the clinician decided which was the most prominent, and only one was entered.

(4) Pathological diagnosis according to a diagnostic test such as a renal biopsy or imaging

Information regarding the composition of the population of the Free State according to the census of 2001 was obtained from Statistics South Africa [1]. The study was approved by the Ethics Committee of the Faculty of Health Sciences, University of the Free State (number 22/06) and the Chief Executive Officer of the hospital. A literature search was done on Pubmed (covering the last 10 years for the epidemiology of nephrology and 5 years for the specific clinical manifestations) to identify similar studies for comparison.

Categorical variables were summarized by frequencies and percentages and analysed using chi-squared tests. Numerical variables were summarized using means and standard deviations and analysed using *t* tests.

Results

One thousand two hundred and sixteen (1216) patients were included in the study. Males and females were approximately equally represented, while the mean age of patients was 40 years (summarized in Table 1).

Table 2 summarizes the racial and gender distributions of the Free State province population of 15 years of age and

Table 1. Description of the study group (13 years of age and older)

	N (%)	Mean age (years) ± SD	Blacks *N* (%)	Whites *N* (%)	Other races *N* (%)
Total	1216 (100)	39.6 ± 15.9	695 (57.2)	437 (35.9)	84 (6.9)
Male	621 (51.1)	40.2 ± 16.5	368 (30.3)	211 (17.4)	42 (3.5)
Female	595 (48.9)	39.1 ± 15.3	327 (26.9)	226 (18.6)	42 (3.5)

Table 2. Race and gender distribution of the Free State province population according to the National Census of 2001 (15 years of age and older) [1]

	Total population (%)	Blacks	Whites	Other races
Total	1 729 270 (100)	1 426 253 (82.5%)	248 964 (14.4%)	54 053 (3.1%)
Male	846 884 (49)	684 986	134 930	26 968
Female	882 386 (51)	741 267	114 034	27 085

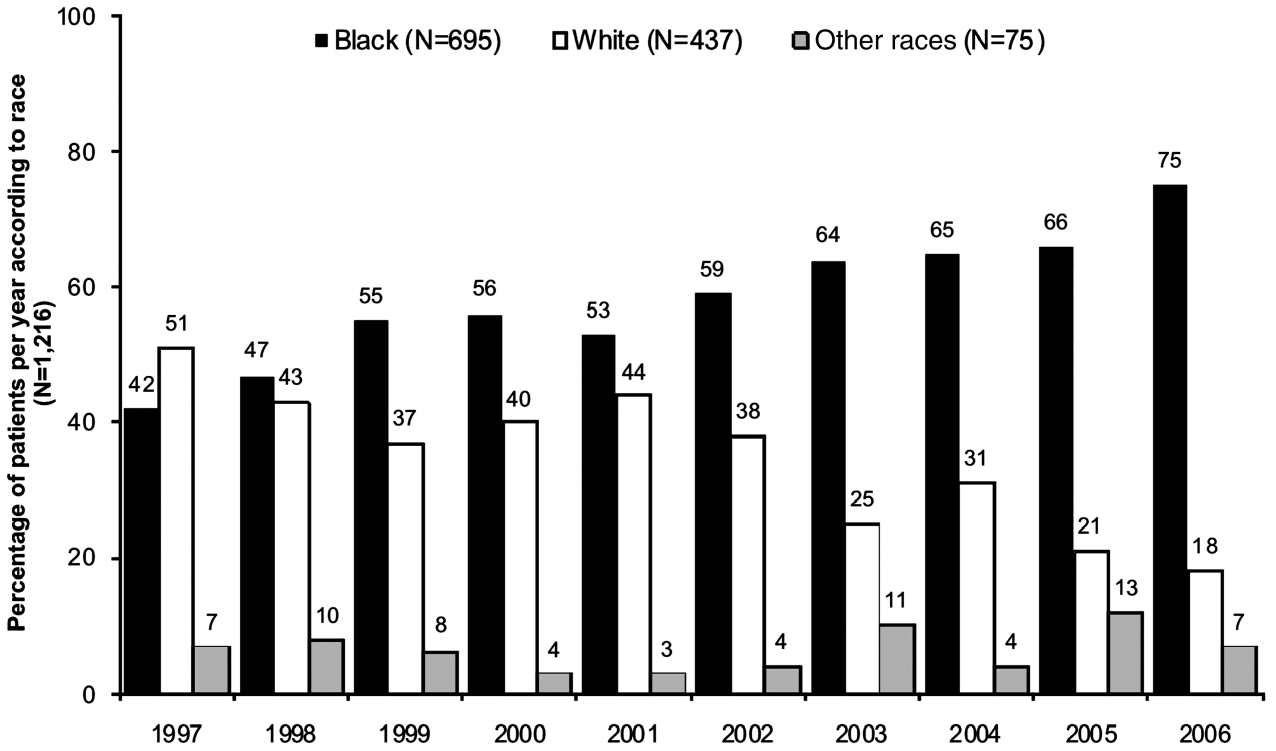

Fig. 1. Racial distribution of referrals for each year (as % of year group).

Table 3. Main presenting clinical manifestations of the study group

Clinical manifestation	Total group *N* (% of 1216) [mean age ± SD]	Blacks *N* (% of specific manifestation) [mean age ± SD]	Whites *N* (% of specific manifestation) [mean age ± SD]
AUF			
Total	128 (10.5) [35.2 ± 15.1]	43 (33.6) [34.2 ± 13.5]	78 (60.9) [35.4 ± 15.6]
Male	57 (4.7) [32.1 ± 15.5]		
Female	71 (5.8) [37.7 ± 14.4]		
Nephritic			
Total	48 (3.9) [26.9 ± 11.0]	35 (72.9) [28.6 ± 11.4]	6 (12.5) [20.8 ± 7.1]
Male	29 (2.4) [25.7 ± 11.3]		
Female	19 (1.6) [28.8 ± 10.6]		
Nephrotic			
Total	203 (16.7) [33.5 ± 16.3]	142 (70.0) [29.9 ± 13.7]	49 (24.1) [43.8 ± 18.5]
Male	115 (9.5) [34.5 ± 17.6]		
Female	88 (7.2) [32.3 ± 14.5]		
ARF			
Total	90 (7.4) [40.4 ± 13.9]	55 (61.1) [38.1 ± 12.7]	27 (30) [46.1 ± 15.0]
Male	40 (3.3) [42.5 ± 14.2]		.
Female	50 (4.1) [38.8 ± 13.5]		
CRF			
Total	461 (37.9) [43.3 ± 14.7]	294 (63.8) [41.0 ± 13.3]	136 (29.5) [48.4 ± 16.7]
Male	270 (22.2) [43.9 ± 14.7]		
Female	191 (15.7) [42.4 ± 14.7]		
Hypertension			
Total	161 (13.2) [40.8 ± 16.2]	84 (52.2) [37.8 ± 14.0]	67 (41.6) [44.9 ± 18.2]
Male	66 (5.4) [41.8 ± 16.2]		
Female	95 (7.8) [40.0 ± 16.2]		

AUF—abnormal urinary findings; ARF—acute renal failure; CRF—chronic renal failure.

older. The ages of the population in the census data from 2001 have been grouped together in five-year intervals, and 15 years was chosen as the youngest age for census data, because it is the closest to the youngest age of 13 years used in our study. Figure 1 shows the changes in the racial distribution of patients per year of referral.

Table 4. Pathological diagnosis of patients where a diagnostic test was available

Pathology	Number of patients (N = 1216)	%
No diagnostic test[a]	838	68.9
Glomerular disease (GD)	242	19.9
FSGS	46	3.8
Minimal change	23	1.9
Membranous	28	2.3
Membranoproliferative	36	3.0
IgA	17	1.4
SLE	35	2.9
Tubulointerstitial disease (TID)	85	6.9
Vascular	39	3.2
Hereditary[b]	51	4.1

[a]One hundred thirty-one (10.8%) patients had diabetes as well, but were infrequently biopsied.
[b]For example, Alport syndrome (included in glomerular diseases) and cystic kidney disease (included in TIDs).

Table 3 represents the main clinical manifestations of the study group. Other races represent only 6.9% of the total study group and were not included in Table 3.

For all conditions, black patients were in the majority except for AUF. The mean ages of black patients with CRF, nephrotic, ARF and hypertension were significantly lower than those of white patients ($P < 0.05$).

Table 4 summarizes the pathological findings in patients with a diagnostic test.

Reports of 12 renal biopsy series were found in the literature, which are summarized in Table 5. No study, similar to the current one, evaluating the whole spectrum of clinical and pathological aspects of renal disease in a particular group of referred patients was found in the literature.

Discussion

The largest group of patients (37.9%) were referred for assessment of CRF, mostly with regard to suitability for renal replacement therapy. Although hypertension was suspected in the majority (51%) of these patients, it was proven histologically in only 2.8%, because a renal biopsy was not done in patients with stages 4 and 5 chronic kidney disease.

Socio-political factors impacting on access to healthcare most likely still had an important influence on referral pattern during the early period of the study. As expected, however, the racial profile of admissions to this unit changed over the years (Figure 1) to reflect the population of the area more closely at the end of the study (Table 2). During this time, changes might as well have occurred as a result of patients preferring to change from the public to the private sector. Some of the referring secondary level doctors are aware of the stringent criteria to qualify for renal replacement therapy in the public sector and might not have referred those patients that they knew clearly did not qualify. This might explain why relatively few patients with diabetic and ischaemic nephropathy, as well as patients older than 60 years of age, were included in the study.

Asymptomatic patients with abnormal urinary findings, presumably having early renal disease, were more likely to be white, while those with advanced CRF were more likely to be black. The studies reported in the literature (Table 5) cannot directly be compared to the current study, with all being renal biopsy series with different indications for renal biopsy. However, the known variation in renal biopsy pathology found from different parts of the world was evident. The main indication for renal biopsy in our study was nephrotic syndrome, and the most prevalent histological diagnosis locally was focal segmental glomerulosclerosis (FSGS), similar to the study reported from Brazil [13], but locally IgA nephropathy was rare. The only secondary form of glomerulonephritis evaluated was systemic lupus erythematosus (SLE), since it appears as a separate group on our histology reports. The other secondary forms (including HIV) were not separated from the primary forms of glomerular diseases in this study. The relatively low number of acute renal failure patients could possibly be attributed to the fact that a large group were referred to the intensive care units and were consequently not included in the study.

In our institution, the majority (37.9%) of patients were seen for the first time late in their disease with CRF, which often required renal replacement therapy, and no definitive diagnosis was possible. With the limited avail-

Table 5. Studies from the literature reporting renal biopsy series (given as percentages)

Ref.	Country	N	AUF	Nephritic	Nephrotic	ARF	CRF	MCD	FSGS	MN	IgA	Mes P	Mem P	Dif P	CN
[7]	Bahrain	498						30	23.8	13.8		5.8	14.3	3.1	2.7
[8]	Romania	635	3.3	21.9	52.3	12.4	10.9	8.5	11.5	11.2		28.9	29.4		7.9
[9]	India	5415		13	65		10.2	11.6	17	9.8	8.6	20.2	3.7		
[10]	Macedonia	1304						7.2	9.9	13.5	11.8	4.4	8.4	12.3	7.4
[10,11]	Spain	9378	25.9	4.5	35.5	12.9	12.1	15.7[a]	12.3[a]	24.2[a]	5.9[a]		6.9[a]		0.4[a]
[12]	China	13 519						0.93	6	9.9	45.3	25.6	3.4		1.9
[13]	Brazil	2096						9.1	29.7	20.7	17.8	3.8	7	2.5	4.1
[14]	Lithuania	316	27.8		29.1				6.8	7.1	15.4		17.9		
[15]	Japan	2832	46.7	10	21										
[16]	Australia	2030							16.9	10.6	34		2.2	1.9	
[17]	Korea	4514						26.6			22.1				
[18]	Czech Republic	3874									34.5				

[a]Patients 15–65 years of age; AUF—abnormal urinary findings; ARF—acute renal failure; CRF—chronic renal failure; MCD—minimal change disease; FSGS—focal segmental glomerulosclerosis; MN—membranous nephropathy; Mes P—mesangial proliferative glomerulonephritis; Mem P—membranoproliferative glomerulonephritis; CN—crescentic nephritis.

ability of dialysis facilities, the need for early detection and preventative measures with regard to renal disease in our area is evident.

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Functional analysis of promoter mutations in the ACTN4 and SYNPO genes in focal segmental glomerulosclerosis

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Abstract

Background. To investigate the promoter mutations of ACTN4 and SYNPO genes in patients with idiopathic focal segmental glomerulosclerosis (FSGS), and to provide functional analysis of these mutations in the role of FSGS occurrence.

Methods. The study consisted of 82 Chinese idiopathic FSGS patients (55 patients had nephrotic syndrome: NS) and 90 healthy individuals. Genomic DNA extracted from peripheral leukocytes of patients of healthy individuals were used to analyse the ACTN4 and SYNPO gene promoter mutations by polymerase chain reaction (PCR) and direct sequencing. Mutations were matched with GenBank and TRANSFAC software database (www.genometix.de; www.gene-regulation.com). A dual luciferase assay system was used to analyse the effects of mutations based on PGL3-Basic vector, pRL-SV40 vector, a PC12 cell line and podocytes *in vitro*. Kidney alpha-actinin-4 and synaptopodin expression of mutated patients and genomic DNA of their parents were investigated.

Results. The study detected the ACTN4 gene promoter 1–34C>T, 1–590delA and (1–1044delT)+(1–797T>C)+