Chronic kidney disease in the elderly: A clinical profile and assessment of disease progression in patients attending renal clinics at tertiary hospitals in Johannesburg, South Africa

Article type: Retrospective, observational study

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirement for the degree of Master of Medicine.

Johannesburg, September 2025

Declaration:

I, Akua Adoma Danso, Student number 2285360, declare that this research report is my own. It is being submitted for the Degree of Masters of Medicine (Internal Medicine) at the University of the Witwatersrand, Johannesburg, South Africa.

This report is submitted in the submissible format as recognized by the Faculty of Health Sciences. It has not been submitted for any degree or examination for any other University.

Dr Akua Adoma Danso

15 September, 2025

The co-author declares that the candidate has made the following contributions to this research paper:

- Substantial contributions to the conception or design of the work; acquisition, analysis or interpretation of data for the work
- Drafting the work and revising it critically
- Final approval of the research paper
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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List of Abbreviations:

AB: alpha blocker

ABC: Abacavir,

ACE-Is: Angiotensin converting enzyme inhibitors

ACE/ARB: angiotensin converting enzyme/angiotensin receptor blocker

AKI: Acute kidney injury

ARBs: Angiotensin receptor blockers

ART: Anti-retro viral therapy

ASA: Aspirin

ATV: Atazanavir

AZT: Zidovudine

BB: beta blocker

BP: Blood pressure

CCB: calcium channel blocker

CHBAH: Chris Hani Baragwanath Academic hospital

CKD: Chronic Kidney disease

CMJAH: Charlotte Maxeke Johannesburg Academic hospital

CVD: Cardiovascular disease

DBP: Diastolic blood pressure

DKD: Diabetic kidney disease

DM: Diabetes mellitus

EFV: Efavirenz

eGFR: Estimated glomerular filtration rate

ESRD: end-stage renal disease

GBM: Glomerular basement membrane

GFR: Glomerular filtration rate

Hb: Haemoglobin

HbA1c: Glycated haemoglobin

HCTZ: Hydrochlorothiazide

HDLc: high density lipoprotein cholesterol

HIV: Human immunodeficiency virus

HPT: Hypertension

ISN-GKHA: The International Society of Nephrology Global Kidney Health Atlas

KDIGO: Kidney Disease Improving Global Outcomes

KRT: Kidney replacement therapy

LDLc: low density lipoprotein cholesterol

LPV/Rit: Lopinavir/ritonavir

NCD: Non communicable disease

PCR: Protein creatinine ratio

RAAS: renin-aldosterone-angiotensin system

SA: South Africa

SBP: Systolic blood pressure

SPRINT trial: Systolic Blood Pressure Intervention trial

SU: Sulfonylurea

TAG: Triglycerides

TDF: Tenofovir

TG: Triglyceride

TSH: Thyroid stimulating hormone

USRDS: United States Renal Data System

WHO: World Health Organization

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Abstract:

Introduction:

Chronic kidney disease (CKD) in the elderly population is common in clinical practice. There are a number of known traditional risk factors associated with CKD progression such as diabetes mellitus, hypertension and proteinuria amongst others. In an elderly cohort from Chris Hani Baragwanath Academic (CHBAH) and Charlotte Maxeke Johannesburg Academic (CMJAH) hospitals these factors were assessed to determine their relationship to CKD and its progression.

Methods:

The purpose of this study was to assess the clinical profile and assess factors associated with CKD progression in elderly patients. A retrospective observational study was performed on 195 elderly patients aged 60-80 years with CKD that attended renal outpatient clinics for a minimum 2 years between 1 January 2010 - 31 December 2018 at CMJAH and CHBAH. Socio-demographics, co-morbidities, biochemical characteristics and aetiologies of CKD (recorded and determined by treating clinicians) were described as proportions. Factors associated with progression of CKD were determined using multivariate logistic regression analysis.

Results:

In a predominantly black population with mean age 66±5years, and M:F ratio 1,4:1 hypertension (94.4%), diabetes mellitus (46.2%) and dyslipidaemia (51.3%) were the leading comorbidities. Diabetes was controlled (HBA1c <7%) in 37 (44%) patients at baseline; blood pressure was controlled (<140/90mmHg) in 62 (31.7%) patients by the end of the second year. Diabetes mellitus was the commonest comorbidity of CKD among progressors. Kidney function declined in 97 (49.7%) patients. The progression rate was -4.8ml/min/1.73m^2 and -5.98ml/min/m^2 in the first and second years of the study. Anaemia was an independent predictor of CKD progression (OR = 1.493, 95% CI: 1.26-1.95, p =0.034). Polypharmacy was observed in 74% of patients.

Conclusion:

Poorly controlled hypertension and diabetes mellitus are common comorbidities in elderly patients with CKD. Anaemia in CKD was independently associated with progression of disease.

Introduction:

Chronic kidney disease (CKD) has a global prevalence of 9.5% and 7.3% in South Africa alone[1]. In persons above the age of 60 (elderly) CKD is commonly encountered[2] and thus the National Kidney foundation (NKF) encourages screening for CKD in all individuals in this age group as CKD tends to be more prevalent in the elderly than in the general population[3].

The natural aging process is associated with changes in the kidney[2, 4]. As early as the 1950s it was found that the estimated glomerular filtration rate (eGFR) declines by 0.75ml/min annually after the age of 40[5]. Non-communicable diseases (NCDs) such as diabetes mellitus (DM), hypertension (HPT) and cardiovascular disease (CVD) are all associated with CKD and often develop in the aged[2, 6]; these diseases superimposed by senescence of the kidney may increase the rate of decline of renal function and more so if these conditions are uncontrolled[6].

The burden of CKD on the healthcare system is substantial and in low- and middle-income countries [7, 8] such as South Africa, the availability of renal replacement therapy (RRT) in the state sector is low[8]. Identifying and managing factors that influence the acceleration of CKD decline in older persons will influence in the reduction of RRT in this population group.

This study describes the clinical profile of elderly persons with CKD and aims to determine factors that are associated with progression of disease in this population.

Methods

Study Design and Setting

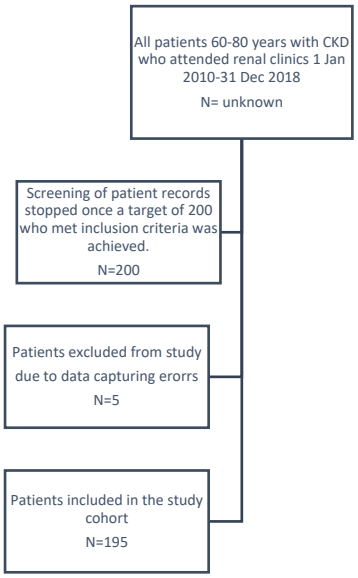
This was a retrospective study of patients who attended the renal outpatient clinics for a minimum of 2 years at CHBAH and CMJAH between 1st January 2010 to 31st December 2018. CHBAH is a 3,400-bed hospital situated in Soweto, Johannesburg and CMJAH is a 1088-bed hospital located in Parktown, Johannesburg.

Ethics

Ethical clearance was obtained from the University of the Witwatersrand's Human Research Ethics Committee (Medical), referenced M191050 (see appendix). Permission to access patient records was given by both the clinical heads of Internal Medicine and Nephrology and the chief executive officers at CHBAH and CMJAH. Direct patient consent was not required, being a retrospective study. However, anonymity was maintained through the use of case identifiers. Overall, the Declaration of Helsinki principles was strictly adhered to in all aspects of the data handling.

Study Population

The study population comprised of diagnosed CKD patients aged 60 to 80 years, at the above hospitals during the period of the study. Patients with acute kidney disease or incomplete medical records of critical data were excluded from the study.



Sample size and sampling Technique

Being a retrospective study, all available data adhering to the study's inclusion criteria was collected, using a convenience purposive sampling technique. Screening of patient records stopped once a target of 200 participants who met inclusion criteria was achieved.

Data Collection

The principal investigator used a data collection sheet to record variables from patient records at baseline presentation, the end of year one, and year two of attendance at the renal clinic. The variables collected include socio-demographics (age, gender, race, alcohol and cigarette use), clinical data (blood pressure, past medical history, medications and pill count), as well as laboratory results (creatinine, electrolytes, full blood count, lipogram, HbA1C, TSH and urine protein creatinine ratio [UPCR]).

Definitions

The following are defined parameters for the study:

1. CKD: eGFR was calculated using the Modified Diet in Renal Disease formula (without race correction) (Table 1).
2. CKD progression defined in accordance with KDIGO CKD guidelines (2012):
   2.1 A drop in GFR staging category (I-V) accompanied by a ≥25% reduction in eGFR from baseline OR
   2.2 'Rapid progression' a sustained decline in eGFR >5ml/min/1.73m2 /year [9]
3. laboratory parameters considered were hypocalcaemia (calcium <2.1mmol/l), hypercalcemia (calcium >2.5mmol/l), hyperphosphataemia (phosphate >1.46mmol/l), hyperkalaemia (potassium >5.1mmol/l), anaemia (Hb <13g/dl in males or <12g/dl in females), and metabolic acidosis (bicarbonate <22mmol/l). Other biochemical variables were excluded due to insufficient data. All laboratory reference ranges were obtained from the National Health Laboratory Service (NHLS).
4. Controlled hypertension: patients with blood pressure <140/90mmHg were considered adequately controlled, in line with the South African hypertension practice guideline guidelines[10].

5. Controlled diabetes mellitus: patients with HbA1C <7% were considered adequately controlled, in line with guidelines SEMSDA[11] and KDIGO[12].
6. Polypharmacy: patients who had ≥5 pill count[13]

Table 1: GFR categories of CKD (adapted from KDIGO 2024[14])

GFR category of kidney disease	Description	GFR (ml/min/1.73m^2)
G1	Kidney damage with normal or increased GFR	≥90
G2	Kidney damage with mild reduction in GFR	60-89
G3a	Mildly to moderately decreased	45-59
G3b	Moderately to severely	30-44
G4	Severe reduction in GFR	15-29
G5	Kidney failure	<15

Data analysis

Data collected from patient records were entered into REDCap® data management software and exported to Microsoft Excel. Analysis was done with IBM-SPSS version 25. Continuous variables were expressed as means ± standard deviations (SD), while discrete variables were reported as percentages. Categorical data was compared using the Chi-square test, while continuous data were analyzed using the McNemar test, Cochran Q, analysis of variance (ANOVA), or *t*-tests as appropriate. Multivariate logistic regression analysis was performed to identify factors associated with the progression of kidney disease. A 95% confidence interval was set and *P*-values <0.05 were considered statistically significant.

Results:

Overview of the study population

A total of 195 elderly CKD patients from CHBAH and CMJAH were included in the study. Table 1 depicts their demographic data. The mean age of the study population was 66±5years (range 60-78). A male preponderance (M:F ratio 1.4: 1) was noted and the majority of the cohort were black (77.4%). Based on clinic records the leading cause of CKD documented by clinicians was hypertension 117 (60%), however, some participants had multiple aetiologies recorded for CKD at the time of their clinical assessment. Although hypertension was noted to be the most common documented cause of CKD by treating clinicians, 184 (94%) of the study cohort were noted in records to have hypertension.

Table 1: Socio-demography, aetiology of CKD, and comorbidities in the study group

Category (N=195)			
Age(years)	66±5		
M:F ratio	1.4: 1		
		N (%)	
Race	Black	151(77.4)	
	White	3(1.5)	
	Coloured	2(1.0)	
	Indian	12(6.2)	
	Unspecified	27(13.8)	
			Unspecified
Social Habits			
	Cigarette smoking	19(14.1)	60(30.7)
	Alcohol	7(5.3)	62(31.8)
	Traditional meds	1(0.8)	64(32.8)
CKD Aetiology	Hypertension	117(60.0)	
	Diabetes Mellitus	86(44.1)	
	Autoimmune diseases	0(0)	
	Obstructive Nephropathy	26(13.3)	
	HIV/AIDS	21(10.8)	
	Others	8(4.1)	
Co-morbidities	Diabetes Mellitus	90(46.2)	
	Hypertension	184(94.4)	
	HIV/AIDS	31(15.9)	
	Malignancy	14(7.2)	
	Dyslipidemia	100(51.3)	
	Cardiovascular disease	53(27.2)	

Clinical and laboratory data

Clinical and laboratory data for the study were collected at three time points: upon baseline presentation, at the end of the first year, and the end of the second year of follow-up at the renal clinic. The distribution of participants according to KDIGO CKD staging can be found in Figure 1. The predominant groups at baseline were stages 3b and 4. The mean values of biochemical and clinical variables are presented in Table 2. There were statistically significant differences in diastolic blood pressure (DBP) (p=0.019), creatinine (p=0.009), albumin (p=0.027), magnesium (p=0.000), and phosphate (p=0.035) over the years.

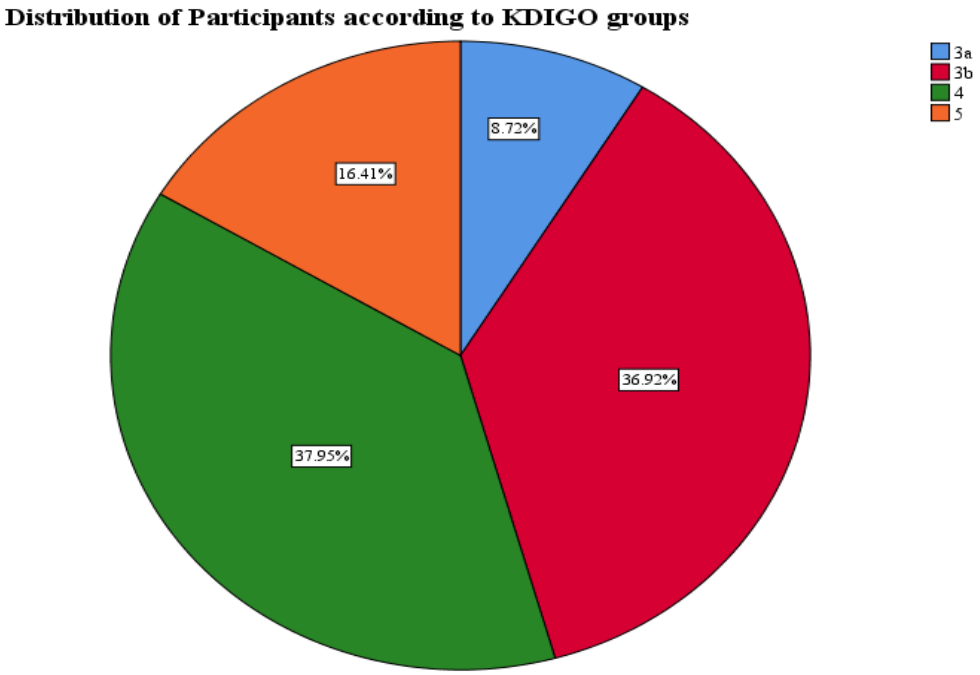


Figure 1: According to KDIGO eGFR CKD categories, many of the participants were group 4 followed closely by group 3b.

Table 2: Analysis of clinical data using Repeated Measures ANOVA across yearly intervals

Variable									Statistics		
	Total***	Overall Mean (SD)	Baseline		Year one		Year two		F value	df	P value
			N	Mean (SD)	N	Mean (SD)	N	Mean (SD)			
SBP (mmHg)	195	149 (16)	195	148 (19)	195	149 (20)	195	148 (20)	0.608	2	0.545
DBP (mmHg)	195	85 (10)	195	86 (13)	195	85 (13)	195	83 (13)	4.018	2	**0.019**
HbA1C* (%)	77	7.59 (1.83)	139	6.94 (1.88)	108	7.29 (7.61)	114	7.61 (2.45)	1.398	2	0.250
LDL (mmol/l)	18	1.91 (0.74)	88	2.44 (1.08)	61	2.19 (0.90)	41	2.11 (1.24)	2.067	2	0.142
HDL (mmol/l)	18	1.10 (0.29)	89	1.32 (0.50)	64	1.28 (0.46)	40	1.21 (0.40)	0.618	2	0.545
TG (mmol/l)	19	2.04 (1.42)	88	1.66 (1.11)	63	1.80 (1.14)	40	1.63 (0.97)	1.564	2	0.223
Potassium (mmol/l)	194	4.85 (0.62)	195	4.80 (0.83)	194	4.85 (0.80)	195	4.89 (0.84)	1.160	2	0.314
Bicarbonate (mmol/l)	195	18.55 (3.33)	195	18.48 (4.29)	195	18.94 (4.17)	195	18.54 (4.63)	0.902	2	0.406
Creatinine (mmol/l)	194	240.74 (147.27)	194	234.05 (152.91)	195	228.83 (145.51)	195	257.65 (198.86)	4.795	2	**0.009**
eGFR**	195	28.98 (18.4)	195	30.38 (41.50)	195	29.26 (13.39)	195	27.31 (13.32)	0.862	2	0.423
Calcium (mmol/l)	184	2.30 (0.23)	190	2.28 (0.21)	191	2.28 (0.21)	189	2.33 (0.54)	1.425	2	0.242
Albumin (g/l)	131	43.2 (3.15)	169	42.32 (5.44)	162	43.78 (4.42)	156	42.78 (4.03)	3.676	2	**0.027**
Magnesium (mmol/l)	91	0.89 (0.09)	125	0.87 (0.13)	121	0.90 (0.13)	99	0.93 (0.14)	10.343	2	**0.000**
Phosphate (mmol/l)	170	1.32 (0.39)	180	1.24 (0.46)	180	1.32 (0.58)	177	1.41 (0.74)	3.394	2	**0.035**
Hb (g/dl)	191	12.2 (1.94)	191	12.05 (2.25)	195	12.20 (2.14)	195	12.19 (2.14)	1.249	2	0.288
TSH mIU/l	15	4.76 (3.46)	85	3.53 (6.50)	41	4.17 (5.46)	50	2.84 (2.04)	0.621	2	0.544

*Only diabetics **derived from MDRD formula without race factor ***Number of participants with complete data over the study period

Assessment of decline in renal function

In the study, progression of CKD in patients was assessed by the use of two separate criteria:

The first criterion considered was 'A drop in GFR staging category (I-V) accompanied by a ≥ 25% reduction in eGFR from baseline'. By the first year, 28/195 patients had progressed. A further 14/195 patients met this criterion at the end of the study (figure 3). McNemar's test showed a significant difference in the proportion of those with renal function decline from baseline to year one and baseline to the end of year two [χ^2 (1) =0.069, p=0.002].

The second criteria considered was 'rapid progression.' i.e., a sustained decline in eGFR of >5ml/min/1.73m^2 /year. Within the first year 33/195 were classified as rapid progressors and a further 64/195 in the second year of the study (figure 4). A McNemar's test showed a significant difference in the proportion of rapid progressors between year one and year two (χ^2 (1) =10.345, p = 0.001).

Overall, 97 (49.75) participants of the study population had progression of CKD by meeting one of the defined criteria. Patients were predominantly ages 60-69years (73.2%; 71/97), with more males (59.8%; 58/97) than females (40.2%; 39/97) [Chi-square: χ^2 (1) =0.141, p=0.707], but this was not statistically significant. The leading co-morbidity in those who progressed was diabetes mellitus (96.9%; 94/97), followed by hypertension (49.5%; 48/97). The yearly decline rate in eGFR from baseline to year one was (-)4.80ml/min/1.73m^2 and (-)5.98ml/min/1.73m^2 from year one to year two.

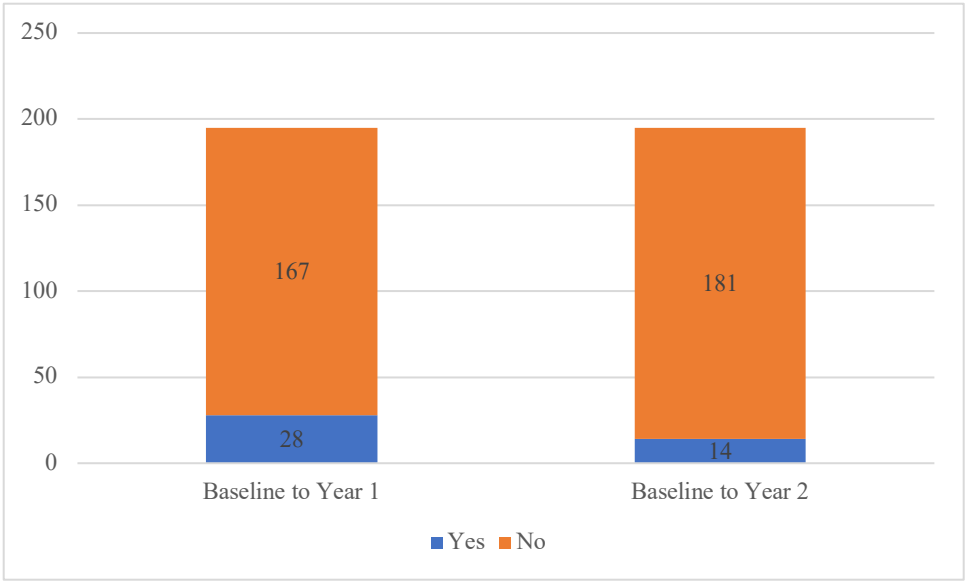


Figure 3: This graph illustrates the number of patients who had CKD progression by drop in GFR staging category accompanied by a ≥25% decline in eGFR from baseline. A total of 42 patients met this criterion for CKD progression (statistically significant difference between the number of patients who met this criterion at the end of years one and two [McNemar's test: χ^2 (1) = 0.069, p = 0.002])

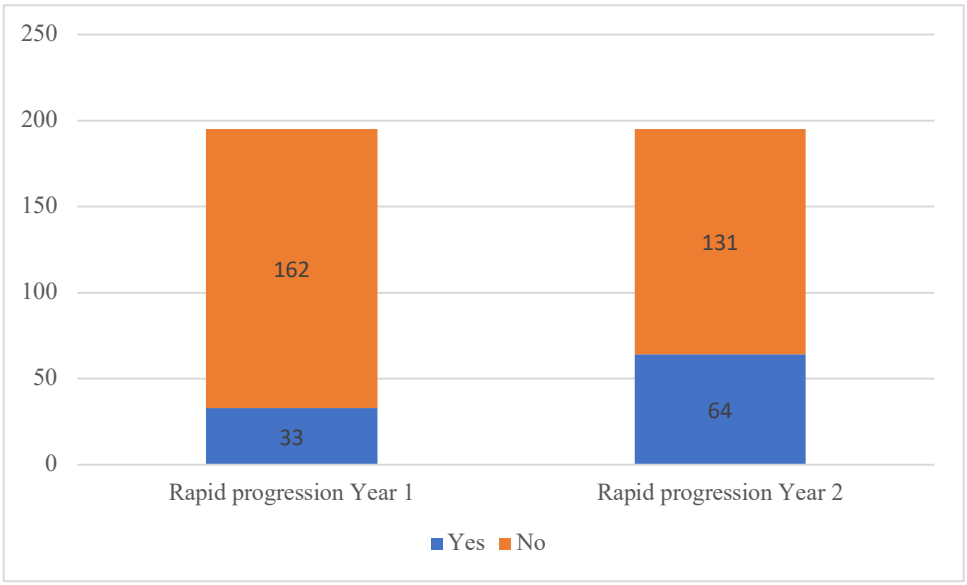


Figure 4: This graph illustrates the number of patients who had 'rapid progression' (eGFR decline of >5ml/min/1.73m^2) of CKD each year. (Statistically significant difference between year one and two [McNemar's test: X2= 10.345, p= 0.001]).

Risk factors associated with decline in renal function

A binary logistic regression was conducted to assess the impact of various demographic, clinical, and laboratory variables on the likelihood of CKD progression. The model included variables such as age, gender, race, medications, and several predefined clinical and laboratory variables targets (Table 3). The overall model was almost statistically significant, χ^2 (8, N = 194) = 9.92, p = 0.05, indicating that the predictors were close to reliably distinguishing between patients who progressed and those who did not. Of the variables assessed, only anaemia, defined as Hb<13g/dl for males or Hb<12g/dl for females was a significant independent predictor of CKD progression (OR = 1.493, 95% CI: 1.26-1.95, p =0.034). This finding suggests that anaemia increased odds of CKD progression by 49.3% in this cohort. Most of the patients with anaemia were in CKD stages 4 (46.5%) and 5 (26.3%), and 43.9% of these patients had progression of disease. No demographic or other clinical and laboratory variable was statistically significant in the model (p > 0.05).

Table 3: Biochemical complications of CKD

Variable	Definition	Yes (N)	No (N)
Hypocalcaemia	Calcium<2.1mmol/l	26	154
Hypercalcaemia	Calcium>2.5mmol/l	11	173
Hyperphosphataemia	Phosphate>1.46mmol/l	46	124
Hyperkalaemia	Potassium >5.1mmol/l	70	124
Anaemia	Hb<13g/dl in males Or Hb<12g/dl in females	114	81
Metabolic acidosis	Bicarbonate<22mmol/l	31	164
*LDL: <1.8 *HDL: female; <1.3 male <1 *Triglycerides: >1.8 *Proteinuria: mild: 0.00 – 0.015 moderate: 0.015-0.05, severe: > 0.05			

*Insufficient (missing) data for further analysis.

Diabetes Mellitus control

Throughout this study, HbA1C values were collected for patients with DM only. Adequate glycemic control in CKD was defined as an HbA1C value <7%. In Figure 5, patients who met this target are reflected. A Cochran Q test was conducted to assess differences in the proportion of patients achieving adequate HbA1c control across three time points (baseline, Year 1, and Year 2). The test showed no statistically significant difference, [Q (2) = 1.520, p=0.468], indicating that the rate of glycaemic control did not change over time.

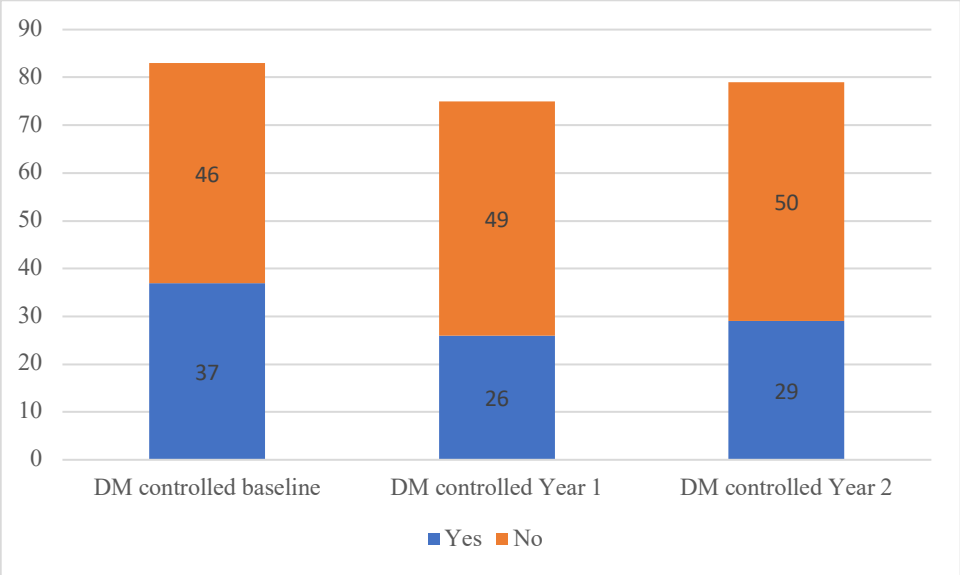


Figure 5: Illustrates the proportion of diabetic patients who met HbA1c target (<7%) over the study period. [Cochran Q test: Q (2) =1.520, p=0.468].

Antihypertensive pill count and Blood pressure control

Figure 6 shows the distribution of antihypertensive pill count (including diuretics) among participants. Several of them were on two, three, or four antihypertensives. A target blood pressure of <140/90 was set to identify participants with controlled blood pressure. Using values at the end of the study, only 62 persons (31.7%) fulfilled the criteria, as shown in Figure 7. A Cochran's Q test was conducted to assess differences in the proportion of patients who achieved BP control across three time points (baseline, Year 1, and Year 2). The test showed no statistically significant difference, [Q (2) =0.205, p=0.903], indicating that the rate of BP control did not change over time. The average number of antihypertensive pills (including diuretics) required to achieve the target blood pressure was 3±1. An independent samples t-test showed that patients who achieved the

target blood pressure (<140/90 mmHg) were not on significantly fewer antihypertensive medications (M = 2.70, SD = 1.1) than those who did not (M = 3.05, SD = 1.1), *t* (191) = -2.02, p = 0.754. Further analysis using a binary logistic regression also revealed that for each additional antihypertensive medication, the odds of achieving target blood pressure decreased by 25% (OR = 0.75, 95% CI: 0.47-0.99, p = 0.047), a statistically significant finding.

Burden of Polypharmacy

At the end of the study, a pill count revealed that the majority of the CKD patients had a high pill burden. Those with polypharmacy (pill count ≥5) were 74.9% of the study cohort. Table 4 presents the distribution of various medications used by the patients, including antihypertensives, diuretics, antidiabetic agents, lipid-lowering drugs, aspirin, and antiretrovirals. The three leading medications in use were calcium-channel blockers (78.4%), furosemide (69.7%), and a statin (66.7%).

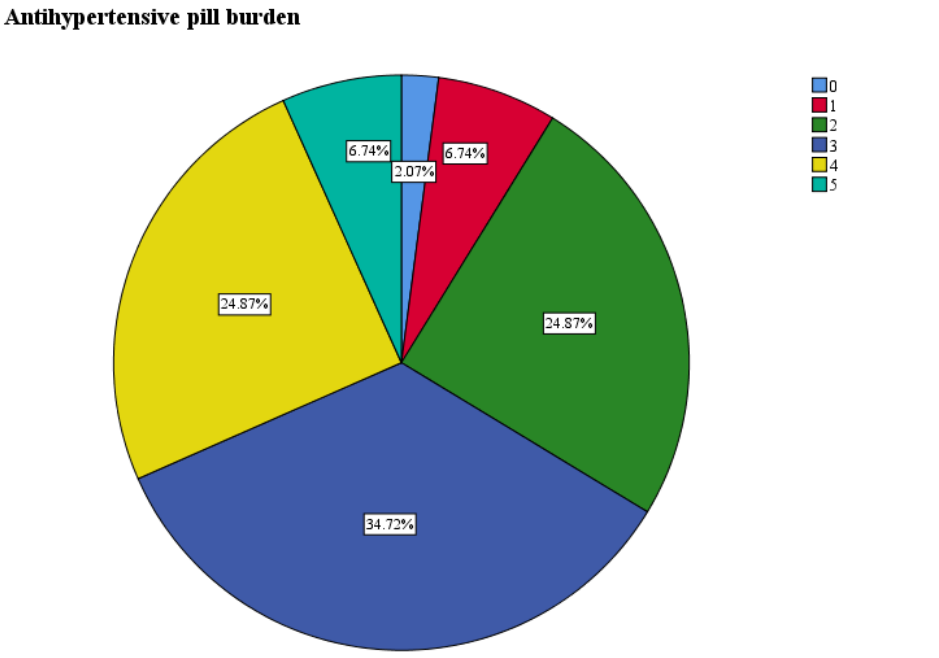


Figure 6: Elderly CKD patients in this study were frequently on two, three or four antihypertensive pills.

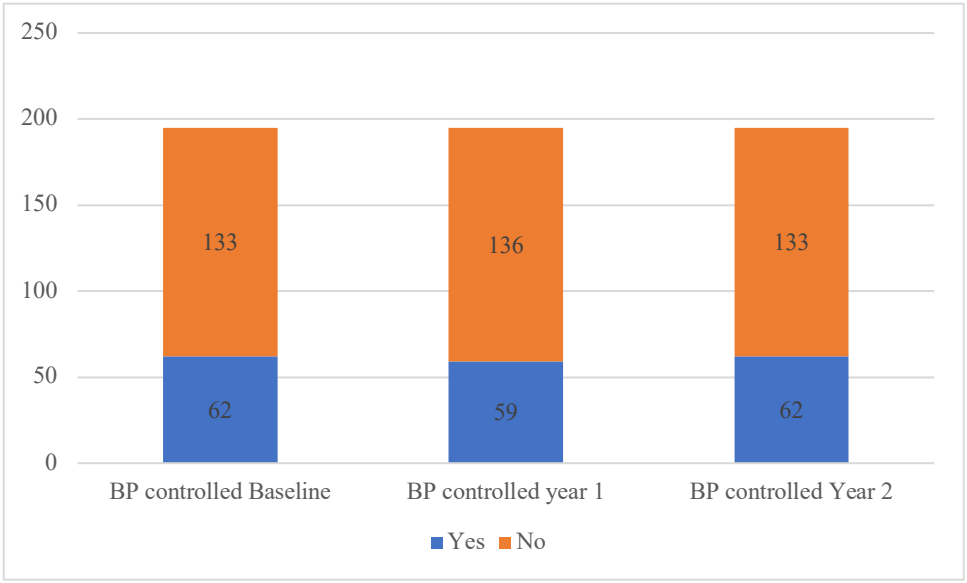


Figure 7: BP control across the years, with no statistically significant difference, [Cochran Q test: Q(2)=0.205, p=0.903].

Table 4: Medication classes and distribution

Class	Count	% (N=195)
Antihypertensive		
AB	93	47.6
BB	59	30.2
CCB	153	78.4
ACE/ARB	110	56.4
Diuretic		
Furosemide	136	69.7
HCTZ	19	9.7
Antidiabetic**		
SU	7	3.6
Biguanide	4	2.1
Insulin	72	36.9
Lipid Lowering Agent		
Statin	130	66.7
Other	0	0
ART		
TDF	0	0
AZT	5	2.6
ABC	29	14.9
LPV/rit	3	1.5
EFV	27	13.8
ATV	0	0
Aspirin		
ASA	81	41.5

AB=alpha blocker, BB=beta blocker, CCB=calcium channel blocker, ACE/ARB=angiotensin converting enzyme/angiotensin receptor blocker, HCTZ= Hydrochlorothiazide, SU=Sulfonylurea, TDF=Tenofovir, AZT=Zidovudine, ABC=Abacavir, LPV/rit=Lopinavir/Ritonavir, EFV=Efavirenz, ATV=Atazanavir, ASA=Aspirin

**DM only

Discussion

This study assessed the clinical and demographic profile of elderly CKD patients attending tertiary renal outpatients' clinics in Johannesburg and investigated factors that are associated with progression of their disease.

The leading co-morbidities of CKD in this study cohort were hypertension (94.4%) and diabetes mellitus (46.2%). This finding is comparable to studies conducted in elderly patients in China [15] and Brazil[16]. There is a paucity of studies on elderly patients with CKD in South Africa, but a local study by Meremo et al had a similar finding of hypertension (96.7%) and diabetes mellitus (38.1%) in slightly younger patients (51- 69 years) who had advanced stages of CKD[17]. It is not surprising that there was such a high prevalence of hypertension in this study cohort considering the bidirectional relationship between hypertension and CKD.

The aetiologies of CKD relied on a clinical diagnosis made by the attending clinician, since the majority of patients did not have a renal biopsy which is considered gold standard for diagnosis.

CKD progression has been defined by different criteria in different populations and this may have an impact on the prevalence of progression and progression rates. In line with the KDIGO 2012 definitions, we considered progression as a drop in eGFR staging category accompanied by a ≥25% reduction in eGFR from baseline or a sustained decline in eGFR of more than 5ml/min/1.73m2 /year (rapid progression). It was found that 97(49.7%) of patients had CKD progression over the study period which is similar to South African[18](49.5%) and Brazilian[16] (56.7%) cohorts.

The rate of decline in this series was -4.8ml/min/1.73m^2 in year 1 and -5.98ml/min/m^2 in the second year. In a Canadian elderly group[19], rates were comparable at -4.2ml to -5.1/min/1,73m^2, however they defined progression of disease as an absolute change in eGFR (eGFR 1 deducted from eGFR 2).

Several factors have been found to be associated with CKD progression; these range from socio-economic, clinical and biochemical components.

The communities we serve are predominantly of black race and this is what is likely reflected in our study population where 77.4% of patients were of black race. Genetically, the APOL 1 gene has been linked to the increased susceptibility of the development of CKD in those of African

descent[20], however this was not investigated in our study series as it was beyond the scope of our study.

The Chronic renal insufficiency study (CRIC) found that males are at higher risk of progression of CKD[21] this may be a possible reason for the male preponderance in our study. Although regression analysis did not predict sex as a factor for progression in this study, more males progressed in disease over time. We were unable to assess the impact of smoking and alcohol consumption in this population due to the degree of missing data, nevertheless, they have been associated with renal decline [18, 21, 22]. Obesity was not assessed in this study, but is considered an important risk for CKD progression[21]. Proteinuria is important in the diagnosis and monitoring of CKD and has been found to be associated with progression of disease in older persons in a number of studies [16, 18, 23]. Unfortunately, we were not able to include proteinuria in regression analyses due to the high degree of missing data for this variable in the study data set.

Traditional risk factors associated with CKD as mentioned above are shared with that of cardiovascular disease and is a significant cause of mortality and morbidity in CKD[24] and in the elderly population[25]. Cardiovascular disease was noted in 27% of patients in this study. This is within the range of what was found in South African populations (17-34%)[17].

Anaemia is a commonly encountered biochemical complication of CKD and in the elderly population[26, 27]. Renal hypoxia secondary to anaemia causes nephron injury through inflammation and fibrosis[28]. The logistic regression analysis performed to identify factors associated with CKD progression showed that anaemia was the only factor that predicted CKD progression in this study series (OR = 1.493, 95% CI: 1.26-1.95, p =0.034). Meremo et al had a similar finding in South African patients(OR 2.1, 95% CI 1.0-4.3, p=0.048)[18].The prevalence of anaemia in this study was 58.4% with patients predominantly CKD stages 4 (46.5%) and 5 (26.3%) and 43.9% of those with anaemia had progression of disease. This is not surprising as anaemia typically occurs in advanced stages of CKD. Findings in a systematic review and meta-analysis were similar, with the prevalence of anaemia in sub-Saharan African countries to be 59.15%[29].

Diabetes mellitus and hypertension are associated with CKD and its progression in the elderly and general populations globally[21, 25, 30, 31]. These conditions were the most prevalent in the study group, however they did not predict disease progression.

Diabetics in this study were consistently uncontrolled over the study period. It is noted that targets for HbA1c in elderly diabetics with CKD should be made on an individual basis to derive the most benefit to the patient and avoid complications from strict glycaemic control. The severity of CKD, hypoglycemic awareness, access to treatment resources and clinical state should be considered in setting the target for each patient.

The KDIGO guidelines for the management of Diabetes in CKD recommend targets for HbA1c of <6.5% to <8% dependent on an individual basis[12]. It is expected that as CKD advances HbA1c improves due to the reduced ability of insulin clearance and renal gluconeogenesis. The majority of our study cohort were CKD stages 3 and 4 at presentation, yet HbA1c worsened over the study period; this is possibly due to patients' resistance to injecting insulin; limited access to other oral agents and newer drugs safer in DM and CKD in the public healthcare system in South Africa.

The prevalence of polypharmacy (5 or more pills) was very high at 74.8%. A systematic review showed that polypharmacy prevalence was 82% (95%CI: 765-86%), and was associated with higher risk of eGFR decline[32]. Kimura et al had similar findings in elderly patients in Japan[33]. Our study did not investigate the relationship between polypharmacy and morbidity or mortality, but it does reiterate the fact that it is a concern even in the South African context. Further analysis of the relationship between polypharmacy and outcomes in this population should be conducted in the future.

In hypertension, the addition of more antihypertensive medication was associated with poor blood pressure control. The high pill burden is likely due to poor adherence to medication and the necessary lifestyle changes.

In this study, a blood pressure control target of <140/90mmHg was met by approximately 30 % of participants. It is important to consider various factors when it comes to blood pressure control. The Systolic Blood Pressure Intervention Trial (SPRINT) [34] found that when a SBP of less than 120mmHg was targeted compared to that of 140mmHg in elderly individuals, reduced rates of all-cause mortality and cardiovascular events were found. Although the benefits of strict SBP control were substantial, adverse events of syncope, acute renal injury occurred more frequently in those assigned to strict SBP control. In an elderly population such as ours, with possible barriers to accessing timeous healthcare intervention, intensive BP targets should be carefully considered.

More research should be performed on elderly patients with CKD and hypertension in low-middle income countries to determine the optimum blood pressure readings that would be most beneficial clinically.

Limitations

The use of secondary data with missing variables was a major limitation in this study. The possibility of reporter bias can also not be excluded, since we relied on records by other clinicians. Inadequate record-keeping prevented the assessment of various clinical variables in this study. The aetiology of CKD was determined by the clinicians who may have different levels of medical expertise. The accuracy of diagnoses could not be confirmed as the vast majority of patients did not have renal biopsies.

Conclusion

CKD is a progressive disease and there are multiple risk factors associated with its decline. In this study hypertension and diabetes mellitus were the most common comorbidities associated with CKD and anaemia in CKD was associated with an increased likelihood of progression of disease.

Recommendations

We recommend further studies in the elderly with CKD in South Africa, to provide evidence-based factors (clinical and otherwise) that can be targeted for better management, which can also stall disease progression in this vulnerable population. We recommend early identification and better control of known risk factors associated with CKD.

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Appendices:

Approved Protocol with Extended Literature review

1.0 Introduction and Literature Review

1.1 Introduction

Non-communicable diseases (NCDs) have become the leading cause of death globally, claiming the lives of approximately 43 million people worldwide and this calls for concern[1]. Every year, 18 million people die from NCDs before the age of 70, and 86% of these deaths occur in low- and middle-income countries[1]. In South Africa (SA), mortality related to NCDs rose by 58,7% over 20 years. The average age at death was 69 for females and 65 for males[2]). The common NCDs contributing to this mortality are cardiovascular diseases, hypertension, diabetes mellitus, and cancer. When complicated, NCDs cause further debilitating illness such as chronic kidney disease (CKD), which in turn worsens the outcome of NCDs.

Due to improving life expectancy globally, the burden of NCDs and their offshoots (such as CKD) is on the rise, posing a challenge to an already constrained public healthcare system, which South Africa has, due to many contributory factors, including a high prevalence of HIV/AIDS. The existing financial burden in the country has limited access to kidney replacement therapy (including chronic dialysis programs) within the public health sector, therefore excluding those who are ineligible for renal transplant from benefiting from these life-saving therapies [3]. This is worrisome when considering the report by Fabian and colleagues[4] of a 6.3% prevalence of CKD among rural South Africans, that is, those who rely more on the government for their healthcare needs.

In response to its impact, multilateral organizations like the WHO have established a Global Action Plan to prevent and control NCDs[5]. This study represents a collaborative effort to cover knowledge

gaps on CKD and its associated factors in South Africa, thereby paving the way for further essential actions towards NCD/ CKD control.

1.2 Prevalence of Chronic Kidney Disease

The International Society of Nephrology (ISN) Global Kidney Health Atlas (ISN-GKHA) compiled updated statistics of kidney disease burden from and care across 200 countries from 2016 to 2022 [6]. The report revealed that the global median prevalence of CKD was 9.5% (IQR 5.9-11.7), highest in Eastern and Central Europe at 12.8%. In South Africa, it was 7.28% (95% CI 6.74-7.78), accounting for about 2.37% (95% CI 2.16-2.53) of deaths in the country [6]. Based on National Health Laboratory Service (NHLS) data for over 6 million South African adults, tested between 2012 and 2016, 1.5% (95% CI 1.4% to 1.5%) were diagnosed with CKD, the majority being females (62.9%) and in stage 3 of the disease [7]. However, in a more recent report between 2017 and 2018, a prevalence of 6.7% (95% CI 5.4 - 7.9) was noted in the country, but with slightly more males (6.6%) than females (6.0%) affected [4].

Hypertension and diabetes mellitus are the leading contributors to the burden of CKD and end-stage kidney disease (ESKD) globally, including South Africa [8].

1.3 Definition and Classification of CKD

According to Kidney Disease: Improving Global Outcomes (KDIGO), CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health. Further CKD classification is based on the cause, glomerular filtration rate category as well as the albuminuria category (Table 1 and 2).

Table 1: GFR categories of CKD (adapted from KDIGO 2024[9])

GFR category of kidney disease	Description	GFR ($ml/min/1.73m^2$)
G1	Kidney damage with normal or increased GFR	≥90
G2	Kidney damage with mild reduction in GFR	60-89
G3a	Mildly to moderately decreased	45-59
G3b	Moderately to severely	30-44
G4	Severe reduction in GFR	15-29
G5	Kidney failure	<15

Table 2: Albuminuria category (adapted from KDIGO, 2024[9])

Persistent albuminuria categories		
A1	A2	A3
Normal to mildly increased	Moderately increased	Severely increased
<3mg/mmol	3-30 mg/mmol	>30mg/mmol

1.4 The Initiation and Progression of CKD

1.4.1 Causes of CKD

The risk factors for CKD can be divided into factors that initiate the development of CKD or those that perpetuate the disease, leading to disease progression [10] is reflected in Table 3.

Table 3: Initiating factors of CKD (Taal and Brenner 2006)

Hypertension
Diabetes Mellitus
Cardiovascular disease
Prior kidney disease
Geographical areas with high prevalence of CKD
Genitourinary Disease
Chronic inflammatory conditions/ auto-immune disease
Iatrogenic causes
Genetic variants associated with CKD
Gestational conditions
Occupational exposures

1.5 CKD in the Elderly: Causes and Management

1.5.1 Diabetes Mellitus

Diabetes mellitus is a leading risk factor for CKD in the elderly population. 1 in 3 adults with diabetes has CKD[11]. The United States Renal Data System (USRDS) in their annual report found that between the year 2017 to 2020, the prevalence of Diabetes amongst individuals above the age of 65 with CKD was 33.2%[12].

Persistent hyperglycaemia leads to the production of free radicals and the activation of inflammatory pathways, with resultant fibrosis and increased vascular permeability of the glomerulus [13]. The podocytopathy that occurs results in albuminuria. In addition, intra-glomerular hypertension is increased and causes further tubular injury, nephron loss, and proteinuria, the hallmark of diabetic kidney disease (DKD) [13].

Management of diabetes and glycaemic targets have been considered in the elderly population. The elderly population is heterogeneous, and chronological age may not reflect true physical or mental fitness. Healthy older persons should be treated to target glycemic goals similar to younger individuals, whereas more frail, chronically ill, or individuals with a shorter life expectancy (<10 years) will require more lenient targets to avoid hypoglycemia or symptomatic hyperglycemia (SEMSDA guidelines, 2017). It is recommended that HbA1c be <7% in adults but up to 8.5% may be acceptable in certain circumstances in the elderly, as mentioned in the SEMSDA guidelines of 2017[14].

1.5.2 Hypertension

The USRDS annual report states that 75.3% of adults over the age of 20 years with CKD have hypertension[12]. Age-related physiological changes contribute to the development of hypertension, which include arteriosclerosis, poor vascular compliance, impaired baroreceptor response, increased central adiposity, and insulin resistance [15].

The management of hypertension in the elderly is significant in preventing cardiovascular morbidity and mortality. Studies have shown the effects of targeting various systolic and diastolic pressures in this population, but the results are controversial. Masoli et al. found that SBP < 120 mmHg was associated with increased mortality and cardiovascular risk in elderly patients. In addition, individuals aged 60 -69 had increased mortality with SBP > 150 mmHg [16]. Garrison et al. analyzed randomized controlled trials conducted in hypertensive patients 65 years and older. They found that the groups with higher blood pressure targets of < 160/90 and < 150/90 did not show any significant reduction in mortality, stroke, or other cardiovascular outcomes compared to those with a lower target of <140/90. Their analysis suggested that there was insufficient evidence to advocate for lower BP targets in the older population [17]. However, Cheung et in analyzing participants from the Systolic Blood Pressure Intervention (SPRINT) trial found that in individuals aged 75 and above, targeting a SBP of < 120mmHg (intensive group) and < 140mmHg (standard group) decreased cardiovascular events (HR 0.66; 95% CI: 0.49-0.90) and all-cause mortality (HR 0.67; 95% CI: 0.48-0.93) [18]. A decrease in eGFR of ≥50% or development of ESKD occurred in 1.1% of the intensive group and 1.2% in the standard group (HR 0.9;95% CI 0.44-1.83) [18].

Locally, the South African Hypertension Society recommends that individuals regardless of cardiovascular risk and underlying comorbidities have a target blood pressure of < 140/90 with the exception of those over the age of 80 years[19].

1.5.3 Cardiovascular disease

Approximately 63% of individuals in CKD stages 1-2 are affected by cardiovascular disease, compared to approximately 75% of individuals when reaching the end stages of CKD. In the advanced stages of CKD, most patients will die of CVD rather than progressing to ESKD [20, 21].

Chronic kidney disease and aging are independent risk factors for CVD, giving rise to a complex interplay of pathologic changes [22]. The cardiovascular risk and related mortality in CKD increase as the renal function declines [20, 21]. Further, as renal function declines, pro-inflammatory processes increase [23]. Metabolic acidosis, reduced cytokine clearance, changes in protein molecules, and systemic disease all contribute to inflammation and lead to endothelial, myocardial, and haemodynamic alterations [23].

The natural process of aging causes changes in the cardiovascular system arising from mechanisms such as changes in endothelial function, oxidative stress, and inflammatory cytokines [24].

The changes that occur with aging in the cardiovascular system include:

- Systolic hypertension and widened pulse pressure
- Heart failure with preserved and reduced ejection fraction
- Valvular and cardiac skeleton calcification
- Atherosclerotic vascular changes

1.6 Changes in the Kidney and Implications for the Elderly

The natural gradual decline in organ systems at both structural and functional levels, known as senescence, is separate from the changes that the kidney undergoes from pathological processes [25-27]. As early as the 1950s, through inulin clearance studies, GFR decline was determined to be 8ml/min/1.73m^2 per decade after the age of 40 years [28]. When superimposed, senescence and acquired diseases (such as hypertension and diabetes) alter this rate of renal decline [27]. Table 4 presents some identified changes in the kidney due to senescence. These may be amplified with coexisting pathology.

Table 4: Changes associated with the ageing kidney (adapted from Alvis et al)

Functional	Micro-anatomical	Macro-anatomical
↓ GFR	Nephrosclerosis	Reduced kidney volume
↓ thirst perception	Nephron hypertrophy	Cysts and tumours
↓ tubular secretions	Reduced number of nephrons	
↓ ability to concentrate urine		

1.6.1 Estimated Glomerular Filtration in the Elderly

Accurate calculation of eGFR is important in the elderly population to avoid overdosing and to renally adjust medication where necessary. Several methods have been developed over the years to calculate eGFR in the general population (Table 5). There is concern that the standardization of the eGFR has led to possible over-diagnosis of CKD in the elderly population, and the conflicting

data available suggests that some methods may be more accurate in calculating eGFR in older individuals [25, 29].

Older literature that has compared the use of various calculations for eGFR in the elderly have different findings. Ferham et al[30] found that in patients 70-110 years the Cockcroft -Gault formula underestimated eGFR compared to that of the MDRD. Years later, Dowling et al[31] found that MDRD and CKD-EPI calculations overestimated creatinine clearance and suggested that the Cockcroft-Gault formula be used in cases where dose adjustment of medication is necessary. Koppe et al[32] extended the argument to say that in the elderly with less advanced CKD BIS calculations should be used and the CKD-EPI in advanced stages.

In contrast, a more A recent systematic review and meta-analysis assessed the accuracy of six frequently used equations in determining the eGFR in older adults, including the Chronic Kidney Disease Epidemiology Collaboration creatinine equation ($CKD\text{-}EPI_{cr)}$ and its combination with cystatin ($CKD\text{-}EPI_{cr\text{-}cys}$), with the Berlin Initiative Study equations (BIS1 and BIS2), and the Full Age Spectrum equations (FAS_{cr} and $FAS_{cr\text{-}cys}$) [33]. The authors reported the BIS and FAS methods as more accurate in determining eGFR than CKD-EPI in the elderly [33].

Table 5: Formulas used to estimate glomerular filtration rate (adapted from Mallappelli et al)

Name of Equation	Comment on the elderly
MDRD	reduced accuracy in older age and eGFR more than 60ml/min/1,73m^2
Cockcroft Gault	Decreased accuracy at less advanced staged of CKD
CKD-EPI$_{cr}$	Overestimates CKD; better in CKD stages 4-5
CKD-EPI $_{cr\text{-}cys}$	Better in estimating GFR
BIS 1-2 / FAS	More accurate than CKD-EPI calculators More accurate in stages 1-3

1.6.2 Complications in the Elderly

Elderly patients with CKD are at significant risk of developing metabolic and nutritional complications [34]. Anorexia associated with uraemia, depression or nutritional losses impacts food intake and causes concomitant weight loss [35]. Furthermore, ageing is associated with changes in body composition and effective metabolism. Adipose tissue redistribution to visceral areas and muscle mass decrease (sarcopenia) occurs [36]. Sarcopenia in CKD is multi-factorial, and ultimately, the various factors converge to cause increased protein degradation and reduced protein synthesis, leading to protein energy wasting [36]. This leads to increased falls and fractures, increased hospitalization and low quality of life [36].

1.7 CKD Progression

Based on KDIGO CKD guidelines (2012), one or more of the following signifies CKD progression:

1. A decline in GFR staging category (I-V). A certain drop in GFR is defined as a drop in GFR category accompanied by a 25% or greater reduction in eGFR.
2. Rapid progression is defined as a sustained decline in GFR of more than 5ml/min/1.73m^2 /year

1.7.1 Mechanism of CKD Progression

There is an interplay between several risk factors and pathophysiological mechanisms that result in CKD progression or the acceleration thereof [10]. These factors are associated with the continual decline in renal function. This can be described as having 3 phases [37]:

1. Acute response to a specific injury, which may be an initiating event of the CKD or a superimposed event
2. Dysfunctional repair of the injury resulting in tissue fibrosis
3. Progressive loss of nephrons

1.7.2 Factors associated with CKD progression

Hyperfiltration states

Systemic hypertension and its associates (obesity, DM, etc) cause an increase in intra-glomerular pressure through the activation of the renin-angiotensin-aldosterone system (RAAS). Increased systemic pressure, especially when prolonged, causes direct injury to the glomerulus, inflammation and eventually fibrotic changes [10].

Reduced nephrons

A reduced renal reserve as a result of low nephron endowment is associated with CKD and progression of disease through haemodynamic changes from the RAAS [10]. Furthermore, the APOL 1 gene mutation, which is most common in Africans, has been associated with reduced nephron endowment, with resultant CKD and its progression [38].

Anaemia

Anaemia in CKD secondary to reduced erythropoietin production more commonly occurs as more renal function is lost. General factors associated with iron, B12 and folate deficiencies, gastrointestinal blood loss, non-steroidal anti-inflammatory agents and other factors may also play a role in all stages of disease. Studies have shown when analyzing cohorts of elderly patients with CKD progression that there is a statistically significant association with anaemia and renal function decline[39-41].

Electrolyte abnormalities

There are numerous electrolyte abnormalities associated with CKD and its progression. As renal function declines, the ability to maintain acid-base and fluid balance, excrete potassium and

phosphorus and function in the maintenance of calcium and vitamin D levels declines (to name a few)[42]. These abnormalities have the ability of causing a range of complications, from bone-mineral density disorders to severe life-threatening scenarios e.g., cardiac arrythmias and death[42].

Proteinuria

An intact glomerular basement membrane (GBM) only allows passage of low-molecular-weight proteins. Local or systemic mechanisms that cause damage to the GBM result in pathological proteinuria and lead to progressive renal injury through inflammation of the tubulointerstitial system and eventual fibrosis [43].

Lipid abnormalities

Dyslipidaemias are associated with CKD progression, including elevated low-density lipoprotein (LDL)/ high-density lipoprotein (HDL) ratios, higher triglyceride levels and low HDL levels [10].

Cardiovascular disease

Cardiovascular disease is a rising complication of CKD that worsens mortality and morbidity in those affected. Both CKD and cardiovascular disease share many risk factors such as obesity, diabetes mellitus, hypertension, dyslipidaemia and others [10].

1.8 Polypharmacy in the elderly

Polypharmacy is generally accepted to be the concurrent use of five or more medications by an individual[44, 45]. As life expectancy increases, so do individuals with multiple co-morbidities. In China, about 70% [46] of elderly patients reported having polypharmacy, 24% in the United Kingdom [47] and 44% in Sweden [48].

1.8.1 Polypharmacy and CKD

The prevalence of polypharmacy among patients with CKD is over 80% [49]. Polypharmacy is associated with poorer clinical outcomes, reduced quality of life and drug-associated adverse events in patients with CKD [49]. A study of older inpatients demonstrated that polypharmacy was associated with an 80% prevalence of drug-drug interactions; the probability of these interactions increased as the number of medications used increased [50].

In the setting of CKD, polypharmacy is associated with increased cardiovascular morbidity and mortality as well as all-cause mortality in older adults. Even though the precise mechanism is unknown, there are documented scientific reports. For example, one prospective study on elderly individuals from the NHANES survey 1999-2018 showed that among the individuals with CKD, 27% (HR = 1.27) and 39% (HR 1.39) had a higher risk of all-cause mortality and cardiovascular disease-associated mortality, respectively, compared with those with no polypharmacy [45]. In another study on adult Japanese patients with non-dialysis dependent CKD, polypharmacy in the context of CKD conferred an increased risk of cardiovascular events and overall increased mortality [44]. Compared to the use of less than five medications, hazard ratios associated with polypharmacy were 2.28 (95CI: 1.00 to 5.21) for kidney failure, 1.60 (95CI:0.85-3.04) for cardiovascular events and 1.25 (95CI: 0.62-2.53) for all-cause mortality [44].

2.0 Hypothesis

Chronic kidney disease in the elderly has a varied aetiology and the progression varies depending on the cause of CKD (individuals with diabetic kidney disease will progress faster than those without diabetic kidney disease).

3.0 Aim

The aim of the study was to determine the aetiology of CKD in the elderly and then to further identify factors that lead to progression of disease.

4.0 Study Objectives

4.1 Primary Objectives:

- To describe the causes of CKD in the elderly population attending renal outpatient clinics at Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Academic Hospital (CMJAH) between 1st January 2010 to 31 December 2018
- Determine the rate of decline in renal function and risk factors that lead to progression of CKD over a two-year period.

4.2 Secondary Objectives:

- To determine the co-morbidities affecting this age group
- To assess the control of diabetes mellitus in the subgroup with diabetes (Hba1c <7%)
- To assess whether blood pressure (BP) in the elderly population is controlled to target levels
- To determine the proportion of patients who achieved optimal BP control

- To determine the quantity of antihypertensive medications per patient needed to control blood pressure (`a blood pressure of less than 140/90 mmHg will be regarded as controlled)
- To assess pill burden and polypharmacy in the elderly

5.0 Methods

This was a retrospective study of patients aged 60 to 80 years who attended the renal outpatient clinics at CHBAH and CMJAH between 1st January 2010 to 31st December 2018 for a minimum of two years.

The following were considered as exclusion criteria:

1. Patients with acute kidney disease
2. Incomplete clinic records of critical data

A data collection sheet was used to record variables from patient records at baseline presentation, the end of year 1 and at the end of year 2 of attendance at the renal clinic. The following clinical data will be collected or assessed for:

<u>Non-modifiable risk factors</u>

- Age
- Race
- gender

<u>Modifiable risk factors</u>

- Hypertension
- Diabetes mellitus

- Dyslipidaemia

  LDL: <1.8 mmol/l

  HDL female; <1.3mmol/l male <1mmol/l female

  Triglycerides >1.8mmol/l
- Cardiovascular disease (ischaemic heart disease, stroke/transient ischaemic attack peripheral vascular disease, heart failure)
- Proteinuria mild: 0.00 – 0.015g/mmol moderate 0.015-0.05g/mmol severe > 0.05g/mmol
- Potassium (hyperkalaemia) >5.1 mmol/l
- Cigarette smoking
- Alcohol ingestion
- Metabolic acidosis (Bicarbonate <22 mmol/l)
- Anaemia <13g/dl males AND <12g/dl females
- Hyperphosphatemia (calcium > 1.45 mmol/l)
- Hypercalcaemia (calcium >2.5 mmol/l)
- Hypocalcaemia (calcium<2.15 mmol/l)

Other co-morbidities:

- Malignancy
- HIV/AIDS

Laboratory variables:

All laboratory results will be obtained from the clinic records and National Health Laboratory Services online application (Labtrak).

The following biochemical factors will be recorded:

- Renal function: Creatinine with calculation of the eGFR using the Modified Diet in Renal Disease formula (MDRD). Potassium levels will also be recorded.

CKD progression defined as one or more of the following: KDIGO CKD guidelines, 2012

  - A decline in GFR category (KDIGO stage I-V). A certain drop in GFR is defined as a drop in GFR staging category accompanied by a 25% or greater reduction in eGFR from baseline.
  - Rapid progression is defined as a sustained decline in GFR of more than 5ml/min/1.73m^2 /year

- Proteinuria: A spot protein-creatinine ratio will be used
- Bicarbonate levels
- Lipid profile
- Full blood count
- Diabetic control will be assessed with glycated haemoglobin (HbA1C)
- Calcium, magnesium and phosphate
- Albumin levels
- TSH
- CD4 count and viral load for HIV infected individuals

Medication history:

Diuretics

- Furosemide
- Hydrochlorothiazide

Anti-hypertensive agents

- calcium channel blockers
- beta-blockers
- alpha-blockers
- RAAS blockers (ACE-I/ARBS)

Lipid lowering agents

- HMG-CoA reductase inhibitors (statins)

Other

- Aspirin

Hypoglycemic agents

- Oral agents (biguanide and sulfonylureas)
- Insulin

Anti-retroviral agents

- Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
- Non-Nucleoside Reverse Transcriptase Inhibitors
- Protease Inhibitors
- Integrase Inhibitors

6. Statistical analysis

Data was collected from patient clinic records and entered into REDCap® data managing software and exported to Microsoft Excel software. Data was analyzed using IBM-SPSS version 25. Continuous variables were expressed as means ± standard deviations (SD) or as medians and

interquartile ranges (IQR) and discrete variables reported as percentages. Categorical data was compared using Chi-square test and continuous data using McNemar test, Cochran Q, analysis of variance (ANOVA) or *t*-tests as appropriate. Logistic regression analysis was performed to identify factors associated with progression of kidney disease. *P*-values <0.05 were considered statistically significant.

7. Ethics

This study made use of information found in the files of patients attending the renal outpatient clinics at CMJAH. The names of patients were removed for privacy. Permission to access patient records was obtained from both the clinical heads of Internal Medicine and Nephrology and the chief executive officers at CHBAH and CMJAH. An application for ethics clearance certificate (M151090) was granted by the University of the Witwatersrand's Human Research Ethics Committee (Medical).

8. Funding

All necessary costs, which include stationery and printing, were funded by the principal investigator.

9.Limitations

This retrospective study was limited by the availability of complete medical records. For the majority of participants, the diagnosis of CKD was made clinically, as a kidney biopsy is

performed in only a few patients at the study centers. Also, the study relied on the records entered by other medical providers (secondary data), therefore, information bias cannot be excluded.

10. Timeline of the study: Gantt chart

	May '19	Sep '19	Feb '20	Dec '21	Jan '22	Feb '25	May '25	Jun '25	Jul '25
Literature review									
Preparing Protocol									
Protocol Assessment/approval									
Ethics Approval									
Data Collection									
Data Analysis									
Write-up									
Assessment									

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Data Collection sheet:

All data recorded in Redcap®)

Record number	
Demographics	age
	sex
	race
Aetiology	Hypertension
(tick relevant box)	Diabetes Mellitus
	Obstructive nephropathy
	HIV/AIDS
	Other
Comorbidities/risk factors	Diabetes Mellitus
(tick relevant box)	Hypertension
	HIV/AIDS
	Malignancy
	Dyslipidaemia
	Cardiovascular disease
Social habits	
Alcohol	yes/no
Cigarette smoking	yes/no
Traditional medication	yes/no

(Data collected at baseline presentation, end of year 1 and end of year 2)

Laboratory results
eGFR ml/min/1.73m2
urine PCR (g/mmol/L)
creatinine (*u*mol/l)
Bicarbonate (mmol/l)
Potassium (mmol/l)
Total cholesterol mmol/l
LDLc (mmol/l)
HDLc (mmol/l)
Triglycerides (mmol/l)
Haemoglobin g/dL
white cell count
platelet count
Corrected calcium (mmol/l)
magnesium (mmol/l)
phosphate (mmol/l)
Albumin (g/L)
HbA1c%
TSH (mIU/L)
CD4 count
HIV Viral load
HIV Viral load undetectable (yes/no)
Average systolic Blood pressure (mmHg)
Average diastolic blood pressure (mmHg)

(Use of medication (yes/no) recorded at baseline presentation, end of first year and end of second year)

Medication
Insulin
Sulfonylurea
Biguanide
Statin
Other lipid lowering agent
Aspirin
Hydrochlorothiazide
Furosemide
Diuretic yes/no
ACE-I/ARB
Beta-blocker
Alpha blocker
TDF+3TC/FTC
AZT+3TC/FTC
ABC+3TC/FTC
Lopinavir/ritonavir
Efavirenz
Atazanavir/ritonavir

Ethics clearance certificate:

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr AA Danso

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M191050

NAME: (Principal Investigator)	Dr AA Danso
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Internal Medicine Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Chronic kidney disease in the elderly. a clinical profile and assessment of disease progression in patients attending renal clinics at tertiary hospitals in Johannesburg, South Africa
DATE CONSIDERED:	2019/10/25
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Drs N Nqebelele and M Mashabane
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/02/19

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **October** and will therefore reports and re-certification will be due early in the month of **October** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

23/02/2020
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

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Leurs R, Church MK, Taglialatela M. H_1-antihistamines: inverse agonism, anti-inflammatory actions and cardiac effects. Clin Exp Allergy. 2002; 32(4):489-498.

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