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Prevalence and progression of chronic kidney disease among adults undergoing creatinine testing in South African public healthcare facilities: a study leveraging data from South Africa's National Health Laboratory Service (NHLS)

Alana T Brennan[1,2,3], **Emma M Kileel**[2,3], **Siyabonga Khoza**[4,5], **Nigel J Crowther**[4,5], **Jacob Bor**[1,2,3], **Matthew P Fox**[1,2,3], **Sydney Rosen**[1,2], **Patricia Hibberd**[2], **Frederick Raal**[6], **Kamy Chetty**[5], **Koleka Mlisana**[5,7], **Jaya A George**[5,8]

[1]Health Economics and Epidemiology Research Office, University of the Witwatersrand Johannesburg, Johannesburg, Gauteng, South Africa

[2]Department of Global Health, Boston University School of Public Health, Boston, Massachusetts, United States of America

[3]Department of Epidemiology, Boston University School of Public Health, Boston, Massachusetts, United States of America

[4]Department of Chemical Pathology, University of the Witwatersrand Johannesburg, Johannesburg, Gauteng, South Africa

[5]National Health Laboratory Service, Johannesburg, Gauteng, South Africa

Correspondence to: Dr Alana T Brennan; abrennan@bu.edu.
ATB and EMK are joint first authors.

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[6]Department of Internal Medicine, University of the Witwatersrand Johannesburg, Johannesburg, Gauteng, South Africa

[7]Academic Affairs, Research & Quality Assurance, National Health Laboratory Service, Johannesburg, Gauteng, South Africa

[8]Wits Diagnostic Innovation Hub, University of the Witwatersrand Johannesburg, Johannesburg, Gauteng, South Africa

Abstract

Background—Chronic kidney disease (CKD) has emerged as a substantial global health challenge, with a marked rise in associated mortality. However, it often goes undetected until advanced stages, particularly in low-income and middle-income countries such as South Africa. We investigated the prevalence and progression of CKD in South Africa, utilising a subset of data from the National Health Laboratory Services Multi-morbidity Cohort.

Methods—This study was a retrospective analysis of adults aged 18–85 years who underwent initial creatinine laboratory testing at government hospitals and clinics from January 2012 to January 2016. CKD was assessed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, excluding the race factor, with a cut-off of CKD-EPI<60 mL/min/1.73 m^2. Lab-diagnosed CKD was defined as two estimated glomerular filtration rate measurements <60 mL/min/1.73 m^2 at least 90 days apart. Cox regression and survival curves were used to estimate HRs and rates of progression.

Results—Among 6 106 521 adults tested between 2012 and 2016, 1.5% (95% CI 1.4% to 1.5%) were diagnosed with CKD, with the majority in stage 3. Over follow-up (median: 2 years, IQR: 0.8–3.6 years), 28.2% (95% CI 27.7% to 28.6%) of patients diagnosed as stage 3a progressed to a more severe disease state. Among patients who were in stage 3b at diagnosis, 29.6% (95% CI 29.0% to 30.1%) progressed and 33.3% (95% CI 32.5% to 34.1%) of stage 4 patients progressed. We estimated a 48% higher adjusted hazard of CKD progression for individuals with diabetes (adjusted HR 1.48, 95% CI 1.41 to 1.57) compared with those without. Advancing age also increased the risk, particularly for those aged >50 years.

Conclusions—This study underscores the urgency for early detection and management of CKD in South Africa, particularly for high-risk individuals. Strengthening primary healthcare systems and raising CKD awareness are vital for improved patient outcomes and to alleviate the burden on healthcare resources. Early intervention can delay CKD progression, thus reducing the need for costly treatments like dialysis and transplantation.

INTRODUCTION

The Global Burden of Disease study reported that the number of deaths attributable to chronic kidney disease (CKD) increased by 41.5% between 1990 and 2017,[1] and more recently, in 2020, the WHO ranked CKD as the 10th leading cause of death worldwide.[2] In 2017, CKD resulted in 2.6 million deaths globally; 1.2 million were a direct result of CKD, and an additional 1.4 million were from cardiovascular disease attributable to impaired kidney function.[1] These estimates likely underestimate CKD burden as they mostly capture deaths due to the most severe stages of kidney failure, which represents only a small

percentage of total CKD-related deaths.[1] Models suggest CKD will become the fifth leading cause of years of life lost by 2040,[3] the majority of which will occur in low-income and middle-income countries, where treatment gaps for kidney disease are most dire.[3]

Studies in sub-Saharan Africa have shown a wide variation in CKD prevalence in adults, with estimates ranging from 2% to 41%, depending on the region and the equation used to define CKD.[4 5] Prevalence in South Africa is estimated to be between 5.9% and 28.9%.[6–11] The high prevalence in South Africa is largely attributable to the country's rise in non-communicable diseases (eg, diabetes and hypertension) compounded by the high burden of HIV and tuberculosis (TB).[12] South Africa also has some of the highest rates of overweight/obesity in sub-Saharan Africa, at 31% for men and 68% for women.[13] Obesity not only exacerbates major CKD risk factors, such as hypertension and diabetes, but is also an independent risk factor for the development and progression of CKD.[14–18]

Managing CKD requires a strong primary healthcare system focused on screening, diagnosis, treatment and management of the disease and its associated comorbid conditions. In South Africa, as in much of sub-Saharan Africa, the health service infrastructure is limited.[19] Consequently, the vast majority of cases are only diagnosed during the advanced stages of kidney disease.[20] Early detection of CKD is likely to improve outcomes[6] while consistent monitoring and initiation of appropriate treatment, can help slow progression to end-stage kidney disease.[21 22] The costs associated with the management of end-stage kidney disease (eg, dialysis or kidney transplantation) are very high, with only wealthier nations being able to adequately fund the treatment of CKD.[4 6] Critical shortages of dialysis equipment and staffing issues are common in low-income and middle-income countries,[23] highlighting the need for prevention and early detection of CKD.[24]

Knowledge of CKD burden could increase awareness, improve early identification and prompt treatment.[25 26] As such, a better understanding of the prevalence and management of CKD in low-income and middle-income countries is urgently needed. We, therefore, sought to estimate CKD prevalence and assess disease progression among patients receiving serum creatinine tests at a government sector hospital or clinic in South Africa using data from South Africa's National Health Laboratory Service (NHLS) database.

METHODS

NHLS cohort creation and description

We used a cohort established through a novel data linkage method previously described.[27] South Africa's NHLS serves as the exclusive provider of laboratory services for the public health system, catering to 80% of the population across all provinces.[28] Due to variations in recording of patient information associated with laboratory tests a single patient may have different sets of identifying data in the database. The data have been linked and anonymised through a graph-based probabilistic record linkage approach. The record-linking methods were expanded to encompass all HIV, TB and non-communicable diseases laboratory tests, to create the 'NHLS Multi-morbidity Cohort'. Using a manual match validation method analogous to the method applied to the HIV laboratory tests,[28] the algorithm validation for

non-communicable diseases laboratory tests yielded a positive predictive value of 95.1% and a sensitivity of 78.3%.

For this analysis, we employed the NHLS Multi-morbidity Cohort, encompassing over 68 million laboratory measurements from more than 30 million unique patients aged over 13 years, each having at least one laboratory measurement between 1 April 2004 and 31 March 2017. The dataset comprises a unique anonymised patient identifier, biological sex, age, laboratory test date, test type, test result, health facility, district and province within South Africa.

CKD primary healthcare evaluation and management guidelines

During the study period, CKD screening guidelines recommended annual screening with serum creatinine for patients considered to be at increased risk for CKD, this included patients with diabetes, HIV infection, hypertension, obesity, patients aged 60 years or older, patients with a family History of kidney disease, among other risk factors.[29] While we do not have information on all potential risk factors for individuals in our cohort, all patients included in this analysis had a screening serum creatinine, so we assume they had at least one of the criteria putting them at increased risk for CKD.

In accordance with the Kidney Disease Improving Global Outcomes (KDIGO) guidelines,[30] we defined CKD as two eGFR (estimated glomerular filtration rate) measurements <60 mL/min/1.73 m^2 at least 90 days but no more than 12 months apart. We calculated eGFR using the Chronic Kidney Disease Epidemiology Collaboration 2009 equation without adjusting for race as this has been shown to lead to overestimations in this population.[31] Stages of kidney disease were classified as stage 1, eGFR≥90 mL/min/1.73 m^2; stage 2, eGFR 60–89 mL/min/1.73 m^2; stage 3a, eGFR 45–59 mL/min/1.73 m^2; stage 3b, eGFR 30–44 mL/min/1.73 m^2; stage 4, eGFR 15–29 mL/min/1.73 m^2; stage 5, eGFR<15 mL/min/1.73 m^2.[30]

Study population

We included patients aged 18–85 years with a first serum creatinine laboratory test performed at a government sector hospital or clinic between 1 January 2012 and 1 January 2016. Each patient had the potential for a minimum of 2 years of follow-up and maximum of 6 years, after their CKD diagnosis. In this prevalence cohort, we included all patients with a laboratory-based diagnosis of CKD.

We identified patients living with HIV as those with an HIV-associated test (CD4 count, HIV viral load, ELISA, etc) any time prior to their first creatinine or up to 12 months after. We identified patients with acute TB infection as those with a positive TB-associated test (ie, culture, smear, GeneXpert, etc) 12 months prior or up to 12 months post creatinine laboratory measurement. HIV-TB coinfected patients were those meeting both the previous definitions. We defined a laboratory diagnosis of diabetes mellitus as a hemoglobin A1c (HbA1c) >6.5%; or fasting plasma glucose ≥7.0 mmol/L or random plasma glucose ≥11.1 mmol/L,[32] 12 months prior or up to 12 months post the serum creatinine laboratory measurement.

Statistical analyses

Clinical and demographic characteristics of the prevalence cohort are presented using simple descriptive statistics. We evaluated CKD progression based on patients last available creatinine measurement within the study period. We defined progression as a drop in eGFR stage accompanied by at least a 25% reduction in eGFR from baseline, in accordance with KDIGO guidelines.[30] Similarly, a patients CKD status was classified as 'improved' if they experienced an improvement in CKD stage and their eGFR function improved by at least 25% from baseline.

To assess rate of transition between CKD stages, we measured average time (in months) between patients' first and last available creatinine measurement. We then calculated total person time (in years) by CKD stage at first measurement and calculated crude rates of progression and corresponding 95% CIs. We calculated crude and adjusted HRs (aHRs) and estimated risk of CKD progression by biological sex, age, diabetes status and HIV/TB status. Finally, we used Cox proportional hazards regression to estimate crude and adjusted rates of progression and corresponding survival curves by subgroups of interest.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

Characteristics of the prevalence cohort

Of the 6 106 521 adults with a creatinine measurement between 1 January 2012 and 1 January 2016, 88 273 (1.5%; 95% CI 1.4% to 1.5%) met our definition of laboratory-diagnosed CKD (online supplemental table 1). The median follow-up time was 2 years (IQR: 0.8–3.6 years). Of those with laboratory-diagnosed CKD, the majority were female (62.9%) and aged 50 or older (70.9%) (table 1). The vast majority of our CKD cohort resided in Gauteng (27.8%) and KwaZulu-Natal (26.2%) provinces (table 1). The prevalence of laboratory-diagnosed diabetes among adults with CKD was 12.8% (95% CI 12.6% to 13.0%), but it is important to note that 75.8% of the cohort did not have a diabetes-associated laboratory measure available within the specified window. Of the 21 338 patients with a diabetes-associated laboratory test performed within ±12 months of their creatinine test, 53.0% (95% CI 52.3% to 53.6%) had laboratory-diagnosed diabetes. 16.5% (95% CI 16.2% to 16.7%) of adults with CKD had documented HIV infection while 5.2% (95% CI 5.0% to 5.3%) had a diagnosis of acute TB infection and 1.4% (95% CI 1.3% to 1.5%) had both.

Of those with laboratory-diagnosed CKD, 38 770 (43.9%; 95% CI 43.6% to 44.2%) were stage 3a (eGFR 45–59 mL/min/1.73 m^2), 25 462 (28.8%; 95% CI 28.5% to 29.1%) were stage 3b (eGFR 30–33 mL/min/1.73 m^2), 14 055 (15.9%; 95% CI 15.7% to 16.2%) were stage 4 (eGFR 15–29 mL/min/1.73 m^2) and 9986 (11.3%; 95% CI 11.1% to 11.5%) were stage 5 (eGFR<15 mL/min/1.73 m^2) at diagnosis (table 1). There were more females diagnosed at stage 3a (65.1%), stage 3b (64.6%) and stage 4 (60.3%), compared with males,

whereas there was less of a difference in sex among those diagnosed at stage 5 (53.4% females vs 46.6% male) (table 1). There were slight variations in the age distribution among individuals diagnosed with different stages of CKD. Among those diagnosed with stage 3a/3b and stage 4, over 50% were >60 years while only 32.2% of those diagnosed with stage 5 were in this age group. 8.6% of patients diagnosed with stage 5 CKD were between 18 and 29.9 years of age, whereas only 3.8% of patients with stage 4, 2.9% of patients with stage 3b and 3.4% of patients with stage 3a CKD were in this age group (table 1). Individuals living with diabetes were more likely to be diagnosed at stage 3b (14.7%) or stage 4 (16.1%) compared with stage 5 (9.7%) (table 1). This might be attributed to other competing health risks. However, it is important to note that the actual percentage of patients with diabetes might be higher as a substantial portion (75.8%) of adults had an unknown diabetes status.

Testing patterns in patients with CKD

Overall, among the 88 273 persons with lab-diagnosed CKD during the follow-up period, 39 484 (44.7%) received their first CKD laboratory-based measure at a primary healthcare clinic and 48 789 (55.3%) at a hospital (table 1). The location of an individuals' first CKD lab measure differed according to their stage at diagnosis. Among those whose first test was in a primary healthcare clinic, 54.2% (95% CI 53.7% to 54.6%) were stage 3a at diagnosis, 29.7% (95% CI 29.3% to 30.2%) were stage 3b, 11.6% (95% CI 11.3% to 11.9%) were stage 4 and 4.5% (95% CI 4.3% to 4.7%) were stage 5 (table 2). In comparison, among those whose first test was in a hospital setting, 35.6% (95% CI 35.2% to 36.1%) were stage 3a at diagnosis, 28.2% (95% CI 27.8% to 28.6%) were stage 3b, 19.4% (95% CI 19.0% to 19.7%) were stage 4, and 16.8% (95% CI 16.5% to 17.1%) were stage 5. Looking by stage of diagnosis, among those who were stage 5 at diagnosis, the majority (82.1%, 95% CI 81.3% to 82.8%) received their first test in a hospital setting, compared with 67.3% (95% CI 66.6% to 68.1%) of stage 4, 53.9% (95% CI 53.3% to 54.6%) of stage 3b, and 44.9% (95% CI 44.4% to 45.4%) of stage 3a patients (table 2).

We analysed the location of patients' second and third CKD lab test to examine potential testing patterns. Although the location of patients' first lab test varied based on their CKD stage at diagnosis, we did not observe much variation in testing patterns, either overall or within specific CKD stages. Table 3 illustrates the location of a patients' second and third lab test, revealing that most patients (51.9%; 95% CI 51.5% to 52.2%) who had their second creatinine test confirming their CKD diagnosis at a hospital, remained at hospital for their third follow-up test. Similarly, 36.2% (95% CI 35.9% to 36.6%) of patients who had their second confirmatory test at a primary healthcare clinic also had a third test at a clinic. These patterns did not vary by CKD stage (table 3). The median time between a patient's first and last creatinine lab was 25.8 months (IQR: 9.8–45.2 months). We observed differences in time between CKD lab measures by stage, with those in stage 5 at first lab having a shorter time between lab measurements compared with those who were stage 3a/3b or 4 (online supplemental table 2).

CKD progression

We evaluated CKD progression by comparing patients' CKD stage at their first CKD laboratory measure to their CKD stage at the last available CKD laboratory measure in the

follow-up period. Movement between CKD stages from patients' first and last CKD lab measure is described in online supplemental table 3. A patient had to experience a drop in eGFR stage as well as a ≥25% reduction in eGFR function to be classified as having CKD progression. Similarly, a patient had to experience an improvement in eGFR stage and a ≥25% improvement in eGFR function for their CKD status to be considered 'improved'. Overall, 55.5% (95% CI 55.1% to 55.7%) of patients experienced no change in their CKD disease status while 18.4% (95% CI 18.1% to 18.7%) improved, and 26.2% (95% CI 25.9% to 26.5%) progressed to a more severe disease state (table 4). Only 3.2% (95% CI 3.0% to 3.3%) of patients who were stage 3a at diagnosis experienced an improvement in their CKD disease status, markedly lower than patients who were stage 3b, stage 4 or stage 5 (table 4). Risk of progression was similar among patients diagnosed at stage 3a (28.2%, 95% CI 27.7% to 28.6%) and 3b (29.6%, 95% CI 29.0% to 30.1%) but slightly higher among patients diagnosed at stage 4 (33.3%, 95% CI 32.5% to 34.1%) (table 4).

When evaluating progression by diabetes status, we saw that people living with diabetes were more likely to progress compared with people without diabetes (table 4). Among people living with diabetes who were stage 3a at diagnosis, 41.7% (95% CI 40.2% to 43.2%) progressed to a more severe disease state. Conversely, among people living without diabetes who were stage 3a at diagnosis, 31.1% (95% CI 29.6% to 32.7%) progressed to a more severe disease state. Similarly, among people living with diabetes who were stage 3b at diagnosis, 40.0% (95% CI 38.4% to 41.5%) progressed vs 29.5% (95% CI 27.8% to 31.3%) of people living without diabetes at the same CKD stage (table 4). The likelihood of progression was similar for people living with versus without diabetes who were diagnosed at stage 4 (table 4). The likelihood of CKD improvement was slightly higher for patients living without diabetes, compared with people living with diabetes, at stages 3a, 3b and 4 (table 4). However, among patients who were stage 5 at CKD diagnosis, we saw a slightly higher likelihood of improvement among people living with diabetes (28.4%, 95% CI 25.6% to 31.3%) compared with people living without diabetes (21.2%, 95% CI 19.6% to 23.0%).

When evaluating the rate of CKD progression, we found that people living with diabetes progressed at a faster rate compared with people living without diabetes (17.1 per 100 person years (PY) vs 13.7 per 100 PY) (table 5). Further, despite having a lower overall risk of progression, males progressed faster than their female counterparts (13.3 per 100 PY vs 11.1 per 100 PY respectively) (table 5). Patients aged 60 years or older progressed at a faster rate than all other age groups (table 5). We saw no difference in rates of CKD progression by HIV and/or TB infection (table 5).

Survival analyses

Survival analyses showed similar trends. Table 5 shows results of crude and aHRs estimating risk of CKD progression compared with no change or improvement in CKD stage. In adjusted analyses, we found that females had an 8.0% decrease in the hazard of progression compared with males (aHR 0.92, 95% CI 0.87 to 0.97) (table 5 and online supplemental figure 1). People living with diabetes had a 43.0% increase in the hazard of progression compared with people without diabetes, adjusting for age, sex and HIV/TB status (aHR 1.43, 95% CI 1.36 to 1.51) (table 5 and online supplemental figure 2). Additionally, among

patients with lab-diagnosed diabetes, those with uncontrolled diabetes (HbA1c >7%) had a 24% increase in the hazard of progression compared with patients with controlled diabetes (HbA1c ≤7%) (aHR 1.24, 95% CI 1.13 to 1.36) (online supplemental figure 3). We also saw an increase in the hazard of progression with increasing age, with the highest hazard of progression among those aged >50 years compared with their younger counterparts (18–29.9 years) (50–59.9 years, aHR 1.36; 95% CI 1.13 to 1.65 and >60 years, aHR: 1.40, 95% CI 1.16 to 1.69) (table 5 and online supplemental figure 4). Patients living with HIV or TB had similar hazards of progression compared with those who had neither HIV nor TB (table 5 and online supplemental figure 5). Moreover, among patients living with HIV, risk of CKD progression was similar among patients with well-controlled HIV (viral load <200 copies/mL or CD4 count >350 cells/mm^3) compared with patients with poor control (online supplemental figure 6).

DISCUSSION

In our study of CKD prevalence, progression and associated risk factors in patients who received creatinine tests in South Africa, the prevalence of CKD was 1.5%. Women and individuals aged 50 years and above made up the majority of the cohort, mirroring global patterns and reflecting age-associated renal function decline.[19 33] CKD prevalence estimates in the current literature vary due to inconsistencies in diagnostic methods and criteria. For example, a recent meta-analysis estimated a pooled prevalence of CKD across six countries in Africa to be 17.8% (95% CI 13.0% to 23.3%), however, all 12 studies included were cross-sectional and relied on a singular eGFR<60 mL/min/1.73 m^2 to diagnose CKD.[5] Relying on a single eGFR estimate likely overestimates the prevalence of CKD by capturing instances of acute kidney injury (AKI). Our study was specifically designed to minimise the misclassification of AKI by using two eGFR measures to diagnose CKD, in accordance with KDIGO guidelines.[30] Our findings are consistent with recent data from a cohort study that similarly used two eGFR measures to diagnose CKD. In this study led by Fabian *et al*, in roughly 2000 South African adults, the crude prevalence of CKD based on two eGFR measures was 0.6%, however, this estimate increased to 6.7% (95% CI 5.4% to 7.9%) when investigators included albuminuria as a diagnostic criterion.[31]

Our data add a critical component to the existing literature by estimating CKD prevalence in a national cohort using two eGFR measures in accordance with diagnostic guidelines. Using a more conservative diagnostic approach than most previously published work, we show that CKD remains a significant concern in South Africa.[34] A notable proportion of patients in our cohort had stage 4 (15.9%) or end-stage kidney disease (stage 5) (11.3%) at diagnosis. The costs associated with the management of end-stage kidney disease (eg, dialysis or kidney transplantation) are exorbitant, with only a few wealthy countries having access to adequate health systems that can meet high demands to treat end-stage kidney disease.[4 6] Critical shortages of dialysis equipment and staffing issues are common in low-income and middle-income countries,[23] once again highlighting that prevention or early detection of CKD is vital in this setting.[24]

This study also shows a concerning trend in the progression of CKD. Over a quarter of all patients with lab-diagnosed CKD progressed to a more severe disease state. Even

more alarming, over one-third (33.3%) of patients diagnosed with stage 4 CKD progressed to the end-stage kidney disease (stage 5). These statistics emphasise an urgent need for consistent monitoring and tailored management strategies, particularly during the early stages of CKD. We found diabetes to be a risk factor for CKD progression in our cohort. People living with diabetes had a 43% higher rate of progression compared with people living without diabetes, after accounting for age, sex and HIV/TB status. The data further reveal that people living with diabetes exhibited a more rapid rate of CKD progression compared with people living without diabetes and that those with uncontrolled diabetes progressed faster than those with controlled diabetes. This difference may be linked to the additional risks and complications associated with diabetes, such as cardiovascular issues. This interconnection between diabetes and CKD emphasises the necessity for a multifaceted approach to CKD management.[35] Furthermore, an observed limitation in the availability of diabetes lab measures could have contributed to an underestimation of the prevalence of lab-diagnosed diabetes among patients with CKD.[36] Such underestimation accentuates the need for more robust screening procedures in subjects suspected of having kidney disease.

The complexity of CKD management extends beyond diabetes alone, and a careful consideration of the interactions between multiple comorbidities, including hypertension and cardiovascular diseases, is crucial. Patients with CKD frequently navigate a landscape of interconnected health conditions that can significantly complicate their care.[37] Consider, for example, a patient with CKD who also suffers from cardiovascular disease but has not been screened for diabetes. Should they succumb to a heart attack before diabetes screening, this would lower the observed incidence of diabetes within the CKD population, leading to an underestimation of the actual need for such screening. This case illustrates how competing risks can obscure the urgency of specific interventions, further emphasising the necessity for an intensified, comprehensive approach to diabetes screening and management among patients with CKD.[35 37]

Our exploration into the testing patterns revealed distinctive differences based on CKD stage at diagnosis. Primary healthcare centres were more likely to diagnose stage 3 CKD while hospitals identified a higher proportion of severe, stage 5 CKD cases. These insights highlight the indispensable role of PHC centres in early detection of CKD and managing comorbidities (eg, hypertension and diabetes) and the vital function of hospitals in diagnosing more advanced stages of the disease. Nevertheless, our study also raised flags concerning the existing patient referral patterns and care settings for those diagnosed with stage 5 CKD. These critical patients require specialised medical attention, which might be inadequately provided if managed at primary healthcare centres rather than specialised hospital facilities. To guarantee the best possible management of CKD, there is an imperative need to bolster healthcare infrastructure and educate healthcare providers about proper referral protocols and care pathways. This will enable a more coordinated and effective approach to treating this complex and serious disease.

The primary strength of our study is the extensive size of our national cohort (n=6 106 521) and the subset with a CKD diagnosis (n=88 273). However, our findings must be interpreted alongside their limitations. First, the probabilistic matching method we employed in cohort creation could be vulnerable to both overmatching and undermatching, potentially

skewing our outcomes in either direction. We did not address missing data because our primary results excluded patients linked to unreliable laboratory results. Even if these patients were included, the main findings would remain stable. For example, assuming that undermatching errors were uniformly distributed, our manual match validation indicates that at the very most, we might be underestimating the prevalence of CKD by 22% (1.0–0.78). Therefore, even adjusting the estimations by 28% (1/0.78) would not significantly alter our overall conclusions. Furthermore, our cohort may be subject to selection bias as many of the patients in our study were tested for CKD during hospitalisation, without detailed information on their diagnoses or reasons for their hospital stays. It is important to note that during the study period, CKD screening guidelines recommended annual screening with serum creatinine for patients considered to be at increased risk for CKD. This included patients with diabetes, HIV infection, hypertension, obesity, patients aged 60 years or older, patients with a family history of kidney disease, among other risk factors. Given that all patients included in our analysis had a screening serum creatinine test, we can infer that they were likely to have at least one of the criteria putting them at increased risk for CKD. Therefore, our cohort may not be representative of the general population and may be skewed towards those with higher risk factors for CKD. Additionally, our study's time frame, spanning 2012–2017, may not reflect recent changes in trends, especially those potentially brought about by the COVID-19 pandemic, which could have altered practices in screening, monitoring and treating CKD and related non-communicable chronic diseases. Lastly, our analysis may be affected by uncontrolled confounding due to the absence of certain patient-level clinical factors in the laboratory data. A linkage of this laboratory data to patient-level clinical information for screening and assessment of additional confounders could enhance the precision and reliability of our analysis.

CONCLUSION

Our study represents, to the best of our knowledge, one of the first large-scale efforts to investigate CKD progression in South Africa. With data on over 6 million adults receiving serum creatinine tests, 1.5% were found to have CKD in accordance with standard guidelines. Of whom, nearly 30% were diagnosed at advanced disease stages. Our study underlines the significance of CKD prevalence and risk of disease progression in South Africa, emphasising its association with diabetes. Our findings advocate for enhanced CKD awareness to facilitate early detection as well as improved diabetes screening and tailored interventions to slow CKD progression. Upgrading healthcare infrastructure and streamlining the referral processes between primary healthcare centres and hospitals are paramount for effective CKD management. Moreover, additional research is required to delve into other factors that may increase progression of CKD, including the role of coinfections and demographic aspects, with a view to devising patient-specific strategies for improved outcomes and minimising the CKD burden in South Africa.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement

No data are available. The data in our study are not publicly available due to the terms of our contract with the NHLS but are available from the NHLS with reasonable request.

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WHAT IS ALREADY KNOWN ON THIS TOPIC

- Chronic kidney disease (CKD) has emerged as a top leading cause of death worldwide. In many low-income and middle-income countries (LMICs), the disease often goes undetected until critical advanced stages.

WHAT THIS STUDY ADDS

- This study represents, to the best of our knowledge, one of the first efforts to investigate CKD progression in South Africa and reveals a concerning trend in the progression of CKD.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- This study emphasises an urgent need for consistent monitoring and tailored management strategies, particularly during the early stages of CKD. Policy-makers can leverage these insights to develop targeted interventions and policies to address the growing CKD burden in LMICs.

Table 1

Demographic and clinical characteristics among individuals with a lab diagnosed CKD between 2012 and 2016, overall and by CKD status

		By CKD stage at first lab			
	Total persons with CKD (N=88 273)	**Stage 3a (eGFR 45–59) (N=38 770)**	**Stage 3b (eGFR 30–44) (N=25 462)**	**Stage 4 (eGFR 15–29) (N=14 055)**	**Stage 5 (eGFR <15) (N=9986)**
Biological sex					
Male	32 766 (37.1%)	13 532 (34.9%)	9005 (35.4%)	5580 (39.7%)	4649 (46.6%)
Female	55 507 (62.9%)	25 238 (65.1%)	16 457 (64.6%)	8475 (60.3%)	5337 (53.4%)
Age (years)					
18–29.9	3445 (3.9%)	1318 (3.4%)	736 (2.9%)	536 (3.8%)	855 (8.6%)
30–39.9	8683 (9.8%)	3807 (9.8%)	2046 (8.0%)	1289 (9.2%)	1541 (15.4%)
40–49.9	13 542 (15.3%)	6113 (15.8%)	3347 (13.2%)	2012 (14.3%)	2070 (20.7%)
50–59.9	18 697 (21.2%)	8293 (21.4%)	5108 (20.1%)	2995 (21.3%)	2301 (23.0%)
>60	43 906 (49.7%)	19 239 (49.6%)	14 225 (55.9%)	7223 (51.4%)	3219 (32.2%)
Diabetes					
No	10 035 (11.4%)	3378 (8.7%)	2621 (10.3%)	1814 (12.9%)	2222 (22.3%)
Yes	11 303 (12.8%)	4332 (11.2%)	3729 (14.7%)	2269 (16.1%)	973 (9.7%)
Unknown	66 935 (75.8%)	31 060 (80.1%)	19 112 (75.1%)	9972 (71.0%)	6791 (68.0%)
HIV/TB status					
HIV−/TB−	67 897 (76.9%)	29 780 (76.8%)	19 605 (77.0%)	10 831 (77.1%)	7681 (76.9%)
HIV+/TB−	14 559 (16.5%)	6454 (16.7%)	4162 (16.4%)	2285 (16.3%)	1658 (16.6%)
HIV−/TB+	4575 (5.2%)	1967 (5.1%)	1342 (5.3%)	757 (5.4%)	509 (5.1%)
HIV+/TB+	1242 (1.4%)	569 (1.5%)	353 (1.4%)	182 (1.3%)	138 (1.4%)
Location of first CKD lab measure					
Primary health centre	39 484 (44.7%)	21 379 (55.1%)	11 727 (46.1%)	4590 (32.7%)	1788 (17.9%)
Hospital	48 789 (55.3%)	17 391 (44.9%)	13 735 (53.9%)	9465 (67.3%)	8198 (82.1%)
Province					
Gauteng	24 545 (27.8%)	11 266 (29.1%)	7008 (27.5%)	3562 (25.3%)	2709 (27.1%)
KwaZulu-Natal	23 107 (26.2%)	9731 (25.1%)	7021 (27.6%)	3875 (27.6%)	2480 (24.8%)
Western Cape	10 737 (12.2%)	4884 (12.6%)	3110 (12.2%)	1680 (12.0%)	1063 (10.6%)

		By CKD stage at first lab			
	Total persons with CKD (N=88 273)	**Stage 3a (eGFR 45–59) (N=38 770)**	**Stage 3b (eGFR 30–44) (N=25 462)**	**Stage 4 (eGFR 15–29) (N=14 055)**	**Stage 5 (eGFR <15) (N=9986)**
Eastern Cape	8386 (9.5%)	3377 (8.7%)	2455 (9.6%)	1536 (10.9%)	1018 (10.2%)
Mpumalanga	6517 (7.4%)	3612 (9.3%)	1642 (6.5%)	781 (5.6%)	482 (4.8%)
Limpopo	4958 (5.6%)	1942 (5.0%)	1393 (5.5%)	891 (6.3%)	732 (7.3%)
North West	4962 (5.6%)	2100 (5.4%)	1374 (5.4%)	828 (5.9%)	660 (6.6%)
Free State	3763 (4.3%)	1434 (3.7%)	1093 (4.3%)	636 (4.5%)	600 (6.0%)
Northern Cape	1298 (1.5%)	424 (1.1%)	366 (1.4%)	266 (1.9%)	242 (2.4%)

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; TB, tuberculosis.

Table 2

Location of first CKD lab measure by CKD stage

	Primary health centre	Hospital	
CKD stage at first lab	**n % (95% CI)**	**n % (95% CI)**	**Total**
Stage 3a	21 379	17 391	
Row per cent	55.1% (54.6% to 55.6%)	44.9% (44.4% to 45.4%)	
Column percent	54.2% (53.7% to 54.6%)	35.6% (35.2% to 36.1%)	38 770 (43.9%)
Stage 3b	11 727	13 735	
Row per cent	46.1% (45.4% to 46.7%)	53.9% (53.3% to 54.6%)	
Column per cent	29.7% (29.3% to 30.2%)	28.2% (27.8% to 28.6%)	25 462 (28.8%)
Stage 4	4590	9465	
Row per cent	32.7% (31.9% to 33.4%)	67.3% (66.6% to 68.1%)	
Column per cent	11.6% (11.3% to 11.9%)	19.4% (19.0% to 19.7%)	14 055 (15.9%)
Stage 5	1788	8198	
Row per cent	17.9% (17.2% to 18.7%)	82.1% (81.3% to 82.8%)	
Column per cent	4.5% (4.3% to 4.7%)	16.8% (16.5% to 17.1%)	9986 (11.3%)
Total	39 484 (44.7%%)	48 789 (55.3%%)	88 273

CKD, chronic kidney disease.

Table 3

Assessment of testing patterns based on location of second (confirmatory) and next available CKD lab measure, overall and by CKD stage

Location of second CKD lab	Location of third CKD lab	N†	% (95% CI)†
Overall, n=72 228*			
Primary health centre	Primary health centre	26 182	36.2% (35.9% to 36.6%)
Primary health centre	Hospital	5209	7.2% (7.0% to 7.4%)
Hospital	Primary health centre	3376	4.7% (4.5% to 4.8%)
Hospital	Hospital	37 461	51.9% (51.5% to 52.2%)
Among those stage 3a (eGFR 45–59), n=32 003			
Primary health centre	Primary health centre	15 090	47.2% (46.6% to 47.7%)
Primary health centre	Hospital	2231	7.0% (6.7% to 7.3%)
Hospital	Primary health centre	1527	4.8% (4.5% to 5.0%)
Hospital	Hospital	13 155	41.1% (40.6% to 41.6%)
Among those stage 3b (eGFR 30–44), n=20 806			
Primary health centre	Primary health centre	7650	36.8% (36.1% to 37.4%)
Primary health centre	Hospital	1583	7.6% (7.3% to 8.0%)
Hospital	Primary health centre	1039	5.0% (4.7% to 5.3%)
Hospital	Hospital	10 534	50.6% (50.0% to 51.3%)
Among those stage 4, n=11 394			
Primary health centre	Primary health centre	2618	23.0% (22.2% to 23.7%)
Primary health centre	Hospital	927	8.1% (7.6% to 8.6%)
Hospital	Primary health centre	542	4.8% (4.4% to 5.2%)
Hospital	Hospital	7307	64.1% (63.2% to 65.0%)
Among those stage 5, n=8025			
Primary health centre	Primary health centre	824	10.3% (9.6% to 10.9%)
Primary health centre	Hospital	468	5.8% (5.3% to 6.4%)
Hospital	Primary health centre	268	3.3% (3.0% to 3.8%)
Hospital	Hospital	6465	80.6% (79.7% to 81.4%)

*16 045 individuals missing information on second or third facility location.

† N (%) calculated out of individuals with available second and third facility location.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

Table 4

CKD progression, overall and by CKD stage at first lab

CKD progression	Overall (%; 95% CI)	Stage 3a (eGFR 45–59) (%; 95% CI)	Stage 3b (eGFR 30–44) (%; 95% CI)	Stage 4 (eGFR 15–39) (%; 95% CI)	Stage 5 (eGFR <15) (%; 95% CI)
Overall					
No change	48 895 (55.4%; 55.1% to 55.7%)	26 613 (68.6%; 68.2% to 69.1%)	10 590 (41.6%; 41.0% to 42.2%)	4811 (34.2%; 33.4% to 35.0%)	6881 (68.9%; 68.0% to 69.8%)
Improved *	16 237 (18.4%; 18.1% to 18.7%)	1227 (3.2%; 3.0% to 3.3%)	7344 (28.6%; 28.3% to 29.4%)	4561 (32.5%; 31.7% to 33.2%)	3105 (31.1%; 30.2% to 32.0%)
Progressed †	23 141 (26.2%; 25.9% to 26.5%)	10 930 (28.2%; 27.7% to 28.6%)	7528 (29.6%; 29.0% to 30.1%)	4683 (33.3%; 32.5% to 34.1%)	–
People living with diabetes					
No change	5720 (50.6%; 49.7% to 51.5%)	2466 (56.9%; 55.4% to 58.4%)	1627 (43.6%; 42.0% to 45.2%)	930 (41.0%; 39.0% to 43.0%)	697 (71.6%; 68.7% to 74.4%)
Improved *	1431 (12.7%; 12.1% to 13.3%)	59 (1.4%; 1.0% to 1.7%)	612 (16.4%; 15.2% to 17.6%)	484 (21.3%; 19.7% to 23.1%)	276 (28.4%; 25.6% to 31.3%)
Progressed †	4152 (36.7%; 35.8% to 37.6%)	1807 (41.7%; 40.2% to 43.2%)	1490 (40.0%; 38.4% to 41.5%)	855 (37.7%; 35.7% to 39.7%)	–
People living without diabetes					
No change	5866 (58.5%; 57.5% to 59.4%)	2250 (66.6%; 65.0% to 68.2%)	1218 (46.5%; 44.6% to 48.4%)	648 (35.7%; 33.5% to 37.9%)	1750 (78.8%; 77.1% to 80.4%)
Improved *	1646 (16.4%; 15.7% to 17.1%)	77 (2.3%; 1.8% to 2.8%)	630 (24.0%; 12.5% to 15.1%)	467 (25.7%; 23.8% to 27.8%)	472 (21.2%; 19.6% to 23.0%)
Progressed †	2523 (25.1%; 24.3% to 26.0%)	1051 (31.1%; 29.6% to 32.7%)	773 (29.5%; 27.8% to 31.3%)	699 (38.5%; 36.3% to 40.8%)	–

*A patients CKD status was classified as ‘improved’ if they experienced an improvement in CKD stage and their eGFR function improved by at least 25% from baseline.

†A patient’s CKD status was classified as ‘progressed’ if they experienced a drop in CKD stage and their eGFR function decreased by at least 25% from baseline.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

Table 5

Crude and adjusted HRs estimating risk of CKD progression versus no change or improvement

Risk factor	N (%) progressed	Total person time (years)	Rate per 100py (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI)*
Sex					
Male	9019 (32.1%)	67 725.1	13.3 (13.0 to 13.6)	ref.	ref.
Female	14 122 (28.2.0%)	127 145.1	11.1 (10.9 to 11.3)	0.88 (0.85 to 0.90)	0.92 (0.87 to 0.97)
Age (years)					
18–29.9	721 (27.8%)	6033.8	11.9 (11.1 to 12.9)	ref.	ref.
30–39.9	1771 (24.8%)	18 036.7	9.8 (9.4 to 10.3)	0.91 (0.83 to 0.99)	1.08 (0.87 to 1.35)
40–49.9	2998 (26.1%)	30 224.5	9.9 (9.6 to 10.3)	0.98 (0.90 to 1.06)	1.24 (1.01 to 1.51)
50–59.9	4873 (23.1%)	42 897.6	11.4 (11.0 to 11.7)	1.17 (1.08 to 1.26)	1.36 (1.13 to 1.65)
60+	12 778 (31.4%)	97 704.6	13.1 (12.9 to 13.3)	1.44 (1.34 to 1.56)	1.40 (1.16 to 1.69)
Diabetes*					
No	2523 (32.3%)	18 480.3	13.7 (13.1 to 14.2)	ref.	ref.
Yes	4152 (40.2%)	24 291.2	17.1 (16.6 to 17.6)	1.48 (1.41 to 1.57)	1.43 (1.36 to 1.51)
HIV/TB status					
HIV−/TB−	17 897 (29.7%)	150 874.6	11.9 (11.7 to 12.0)	ref.	ref.
HIV+/TB−	3761 (29.2%)	31 006.5	12.1 (11.7 to 12.5)	1.03 (1.00 to 1.07)	1.04 (0.97 to 1.11)
HIV−/TB+	1179 (29.0%)	10 297.0	11.4 (10.8 to 12.1)	0.97 (0.91 to 1.03)	0.97 (0.87 to 1.09)
HIV+/TB+	304 (27.5%)	2719.2	11.2 (10.0 to 12.5)	0.99 (0.88 to 1.11)	0.97 (0.78 to 1.19)

*Among those with a diabetes lab (n=22 025).

CKD, chronic kidney disease; PY, person-years.