The Burden Of Unrecognized Chronic Kidney Disease In Patients With Type 2 Diabetes At A County Hospital Clinic In Kenya: Implications To Care And Need For Screening

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Abstract

Background : Chronic Kidney Disease (CKD) in patients with type 2 diabetes enhances the risk of cardiovascular events and a strong predictor of progression to end-stage kidney disease. Early diagnosis is encouraged for referral to specialist kidney care for active management that would optimize outcomes including forestalling progression to end-stage kidney disease. This study was conducted in a regional public health facility in Central Kenya with a high prevalence of type 2 diabetes. It was aimed at determining the burden of undiagnosed chronic kidney disease in their clinic of ambulatory patients with type 2 diabetes who dwell mainly in the rural area.

Methods : A cross-sectional study was conducted at the out-patient of Nyeri County hospital. A total of 385 patients were enrolled over five months. Informed consent was obtained and clinical evaluation was done, a spot sample of urine obtained for albuminuria and venous blood drawn for HbA1c, Lipids and serum creatinine. Estimated GFR (eGFR) was calculated using the Cockroft-Gault equation. Chronic kidney disease (CKD) was classified on KDIGO scale. Albuminuria was reported as either positive or negative. Main outcomes measure: Estimated Glomerular filtration rate and albuminuria as markers of chronic kidney disease.

Results : A total of 385 participants were included in the study, 252 (65.5%) were females. There were 39.0 % (95%CI 34.3-44.2) patients in CKD/KDIGO stages 3, 4 and 5 and 32.7% (95%CI, 27.8-37.4) had Albuminuria. The risk factors that were significantly associated with chronic kidney disease/KDIGO stages 3, 4 and 5 were: age >50years, long duration with diabetes >5years and hypertension. Employment and paradoxically, obesity reduced the odds of having CKD, probably as markers of better socio-economic status.

Conclusion : Previously unrecognized CKD of KDIGO stages 3,4 and 5 occurred in over thirty percent of the study patients. They were at high risk of progression to end-stage kidney disease and cardiovascular events. The risk factors of hypertension, age above 50, long duration of diabetes should help identify those at high risk of developing CKD, for screening and linkage to care. The imperative of screening for chronic kidney disease is availing care in publicly-funded hospitals.

Background

Approximately 40% of patients with diabetes, in their lifetime, develop Diabetes Kidney Disease defined by impaired or falling Glomerular Filtration Rate and/or albuminuria. *(1)* Additional development of CKD on diabetes greatly enhances the risk of cardiovascular events and poor cardiovascular outcomes. *(2, 3, 4, 5).*

The UKPDS *(6)* demonstrated that after median follow up of 15 years, 38% of the study patients previously with normo-albuminuria and 29% normal GFR developed albuminuria and impaired GFR respectively. The time span to kidney events may certainly be shorter in real-life and non-trial clinical care

conditions, probably more so in sub-Saharan Africa where the challenges to organization and provision of care limit achievement of optimal care for so many patients.

CKD in type 2 diabetes is a subtle disease in early phases, but when it becomes manifest, it is severe. Patients seek care when prompted by symptoms. However, access to care is considered insufficient until those at high risk of developing CKD are screened and case identification established as a standard of care.

That CKD is defined by albuminuria and/or impaired eGFR is important because they are relatively easy to measure though not routinely done or reported. In Kenya, indeed in sub-Saharan Africa, early and timely case-finding and access to care are challenges occasioned by scarce resources and non-integrated healthcare systems which can still be overcome. End-stage kidney disease is much worse: it is costly *(7, 8)* and carries high mortality*, (9)* therefore secondary prevention strategies should be strengthened.

The context of the study is that public hospitals have challenges of healthcare provision at the level of clinical staff and the care support within the facilities, especially laboratories and pharmacies. Therefore, it is presumable that secondary prevention is sub-optimal in the patients who use such facilities.

Methods

Study design: A cross-sectional analysis of adult patients with type 2 diabetes without overt complications or co-morbidities attending the out-patient diabetic clinic.

Sample size determination. Prevalence of Cardiovascular risk factors in type 2 diabetes, and this included chronic kidney disease, and the prevalence of hypertension was used to determine the sample size, $N = 1/d^2 * (Z^2 \times P (1-P))$

N = Sample size, Z—1.96 (95% confidence interval), P = Estimated proportion of hypertension in type 2 diabetes patients = 50%, d = Margin of error (precision error) = ±5%, substituting into the formula, N = 384.

Study setting: The study site is a public hospital in Central Kenya, a region of higher prevalence of type 2 diabetes. The diabetes clinic is run every Friday morning each week except on public holidays. About 100 patients with either type 1 or 2 diabetes mellitus are seen on each clinic day by a Medical officer, registered Nursing staff and occasionally, a consultant physician. Booked patients receive clinical reviews that include but not limited to, weight and Blood Pressure measurements, diabetes education and blood glucose assays. Serum lipids, creatinine, and Albuminuria tests are not routine for patients on a clinic day.

Study Population: Adults with file diagnosis of type 2 diabetes, aged >30years, on follow-up in the clinic for not less than 6 months and on anti-diabetic treatment.

Exclusion criteria: Patients excluded were/had type 1 diabetes mellitus or type 2 diabetes who had been hospitalized in the previous 1 month prior to the index clinic visit, file diagnosis of heart failure or chronic

kidney disease, secondary diabetes mellitus and those with type 2 diabetes who declined to give consent to participate.

They were enrolled on consecutive clinic days over nearly five (5) months between November, 2014 and early March 2015.

Sampling, recruitment and data collection: The investigators went through the files before the start of the day's clinic session and selected all eligible patients. The eligible participants, on each morning of the clinic day, were assigned random numbers and then systematically selected. Each patient who met the inclusion criteria was given full explanation of the study and enrolled after giving written informed consent.

Socio-demographic information of age, gender, occupation, level of education, duration of diabetes, and treatment history (of hyperglycaemia, hypertension, and lipid disorder) and any other illnesses were documented. Chart/file review was done to corroborate the information. HIV status was enquired and all the patients interviewed reported a negative status. Marital status, level of formal education, alcohol intake and cigarette smoking were recorded.

Full clinical examination was done; weight and height were measured and BMI calculated as Weight (kg) divided by square of Height (m^2). Waist and hip circumferences were also measured in centimeters. Blood Pressure was determined using a manual mercury sphygmomanometer, the standard way, after the patient had rested for not less than ten (10) minutes. Diagnosis of hypertension was made at BP ≥140/90mmHg, and classified per JNC 8*. (10)*

Laboratory: A 10-ml venous blood sample was drawn from the antecubital fossa, of which a 2-ml blood sample was processed in an EDTA-anti-coagulated bottle for HbA_1c determination. *HBA1c* was processed by glycol-hemoglobin ion exchange resin method from *ERBA MANNHEIM Gmbh* at the laboratory. HbA1c>7.0% was considered sub-optimal control. The other 8-ml blood sample was processed in a plane bottle and transported for automated assay of serum creatinine and lipids.

Lipid profile was analyzed using *Human Gmbh* kit. Total cholesterol was measured using the CHOD-PAP method based on Trinders Methodology, a calorimetric, enzymatic test for cholesterol with lipid clearing factor. HDL cholesterol was measured using human cholesterol liqui-color Phosphatungstic Acid method, end-point kit. *GPO-PAPA METHOD,* a colorimetric, enzymatic method with glycerophosphate oxidase was employed to assay the triglycerides.LDL-cholesterol was computed from the formula: [LDL-chol] = [Total chol]—[HDL-chol] - ([TG]/2.2) where all concentrations are given in mmol/L. LDL-Cholesterol above 2.0mmol/L was considered higher risk level.

From the serum creatinine results, estimated glomerular filtration rate was calculated on Cockroft-Gault formula:

$$\text{GFR - Cockcroft - Gault} = \frac{(140 - \text{age} \times \text{body weight})}{\text{serum creatinine} \times 0.814 \text{ for males}}$$

The results were the multiplied by 0.85 for females; where age is in years, weight in kg and serum creatinine in micromol/L. *(11).*

SPOT urine was obtained from each participant in the morning of the clinic day. This sample was used for Albuminuria determination semi-quantitatively as *Urinary albumin to creatinine ratio,* using the *CLINITEK Microalbuminuria reagent strips.* CLINITEK Micral–2 Strips, dipped in freshly-voided urine sample, provide semi-quantitative albumin-to-creatinine ratio results in one minute. A single spot urine test has been demonstrated as reliable, *(12)* and has been shown to compare well with the gold standard, 24-hour urinary albuminuria. *(13).*

Statistical analysis. Categorical data (gender, age categories, socio-demographics, habits of alcohol-intake and cigarette-smoking and other clinico-laboratory categories-especially eGFR categories/stages) were summarized as proportions and continuous ones as mean (+/-SD), median and interquartile range. Differences in mean +/-SD between the socio-demographic and clinical characteristics of the patient groups were analyzed using student t-tests. Chi-square and odds ratios (OR), where applicable were used for association of variables with chronic kidney disease. Logistic regressions were done on variables where/when p-value was significant, $p<0.05$, in bivariate analysis. The odds ratios (OR) were expressed in 95% confidence intervals and p-value was significant at $p \leq 0.05$. These were analyzed on the statistical software, SPSS version 20.0.

Results

Figure 1 summarizes the recruitment flow of the study subjects. Three hundred and eighty-five (385) patients with type 2 diabetes in ambulatory setting were included in the study.

Table 1 shows socio-demographic and treatment information of the study subjects. The population mean age was 63.3 years, IQR of 56–71years. The males were significantly older, 65.7(13.7) years than the females, 62.1(12.0) years. The proportion of females with obesity (BMI $\geq$ 30kg/m^2) was 26.2%, compared to males at 15.0%, and similarly, more females than males had obesity when waist circumference was used.

Two hundred and thirty-three, 60.5% of the study subjects had poor glycaemic control and191 (49.6%) had hypertension where more than 75.0% of them were poorly controlled. The proportion of males and females with optimal control of hypertension and glycaemia were similar. However, the lipid parameters of total cholesterol and LDL-cholesterol were higher and HDL-cholesterol lower in the females.

The proportions of the study subjects with CKD in the various KDIGO stages (by eGFR) were: *G1* (>90ml/min/1.73m^2)- 20%, *G2* (60–90ml/min/1.73m^2)–41%, *G3a* (45–60ml/min/1.73m^2)–21% and *G3b* (30–45ml/min/1.73m^2)–12.5%, *G4 (*15–30ml/min/1.73m^2)–4.7%, and *G5* (<15ml/min/1.73m^2)–0.8%. One hundred and fifty, 39.0% of the study patients had eGFR<60ml/min/1.73m^2 while one hundred and twenty-six, 32.7% of them had Albuminuria. There were no gender differences in the proportions of subjects with albuminuria and those in the various CKD/KDIGO stages.

Table 2 shows treatment choices of the study patients, 68.1%, were on oral agents-only and 29.1% were on insulin-based therapy, either as combination with oral agents (12.0%) or insulin-only (17.1%). Use of ACEi/ARBs for hypertension treatment was documented in 69.0%. Over 80% of the subjects made four or more clinic visits in the previous 12 months. Over two-thirds, (68.1%) of the patients were on oral glucose-lowering Agents (OGLAs), 17.1% were on insulin-only and 12% on insulin-OGLA combination. Only 12.5% of the patients were on statins. Over 75% of the study patients attended the clinic 4–5 times or more, in the previous 12-months. Two in three, 69% of the patients treated for hypertension were on either Angiotensin Converting Enzyme Inhibitors (ACEi) or Angiotensin receptor blockers (ARBs).

Table 3 shows bivariate analysis of subjects in the early Chronic Kidney Disease (CKD) Stages 1 and 2 compared to those with advanced CKD in Stages 3, 4 and 5. The mean age of the patients with advanced Chronic Kidney Disease (eGFR<60 *ml/min/1.73m$^{2)}$* was 70.8 years compared with 58.6 years of those in early CKD stages 1 and 2. The subjects in early CKD stages 1 and 2 had markers of better socio-economic status (namely, higher level of formal education and employment) than their counterparts with advanced CKD stages 3, 4 and 5. The mean SBP was higher (148.8mmHg vs. 140.3mmHg), and duration of diabetes was longer (11.0 versus 5.0 years) in patients with advanced CKD/KDIGO stages 3, 4 and 5 compared to those in early CKD/KDIGO stages 1 and 2. Gender did not increase the odds of occurrence of advanced CKD stages 3, 4 and 5, as the proportions were not significantly different between females (36.9%) and the males (42.9%), (p>0.05).

The patients in either of the CKD groups had similar glycaemic control and mean diastolic blood pressure. Obesity (BMI≥30kg/m^2) paradoxically reduced the odds of having advanced CKD (eGFR<60 ml/min/1.73m^2).

Table 4 shows logistic regression of the risk factors of higher stages of CKD (eGFR<60 ml/min/1.73m^2) and their adjusted Odds Ratios (OR) that were significant at bivariate analysis. Age above 50 years, longer duration of diabetes >5 years, systolic blood pressure ≥140mmHg and obesity (BMI≥30kg/m^2) were significant determinants of Chronic Kidney Disease (eGFR<60 ml/min/1.73m^2).

Age, marital status, education level, employment status, duration of diabetes in years, obesity of BMI ≥30 kg/m^2 and hypertension were included in the logistic regression model. Age, duration of diabetes above 5 years, hypertension (as both continuous and categorical variables) were found to increase the odds of having CKD/KDIGO stages 3 to 5, but obesity (by BMI) mitigated the risk of having Chronic Kidney Disease in the study patients.

Table 5 shows risk factor loading and the change in the odds of having advanced stages of Chronic Kidney Disease (eGFR<60 ml/min/1.73m^2). Hypertension alone increased the odds by three times (x3), but addition of glycaemic control (HbA1c), age above 50 years, duration of diabetes >5 years and cigarette-smoking increased the odds by six times (x6).

Discussion

The prevalence of CKD stages 3 to 5 in this adult population who were 30yrs and above, with type 2 diabetes, was 39.0% (95%CI, 34.3–44.2) by eGFR (<60 ml/min/1.73 m^2) and 32.7% (95%CI, 32.7–37.4) for albuminuria. Focusing on each CKD-stage, 33.5% were in stage–3, 4.7% in stage–4 and 0.8% in stage–5 in this study. The occurrence of CKD was previously unknown to both the patients and healthcare providers. These stages of CKD are often asymptomatic, so patients do not promptly seek care. The stages are only detected when appropriate tests are done.

The policy of cost-sharing in public health facilities may have limited access to both clinical care and laboratory diagnostic services of the patients who could not afford them. This study excluded any patients who had recently been discharged from hospital; therefore, the prevalence reported is an underestimate.

The meta-analysis of studies on diabetes kidney disease in sub-Saharan Africa by Noubiap JJ et al *(14)* gave a summary on methods used and characteristics of the patients involved in those studies, mentioning some shortcomings that limited adequate comparability. Several of those studies included patients with type 1 and 2 diabetes, conditions with fairly divergent time paths towards evolution of kidney disease, even when risk factors may be common.

In this study, we discuss the prevalence CKD stages 3 to 5 in context of its magnitude, clinical significance, opportunities of case-finding and implication to care needs.

Studies to determine the prevalence of CKD stages 3 to 5 and/or albuminuria in patients with type 2 diabetes in sub-Saharan Africa have found a wide range of figures. Our own study on patients with type 2 diabetes for less than 2 years but relatively younger, in a tertiary hospital, found 26% had albuminuria. *(15)* Ngassa et al, in S. Africa found 33.6% of their patients had proteinuria and 17.3% had CKD of stages 3, 4 and 5 (eGFR<60 ml/minute/1.73m^2), aggregated for both type 1 and 2 diabetes.*(16)* The prevalence of CKD in patients with type 2 diabetes was 41.1% in a Nigerian study.*(17)* Advanced CKD, of eGFR<60 ml/min/1.73 m^2, was found in 18.2% and 23.8% of subjects with diabetes using the MDRD and Cockcroft-Gault (C-G) equations respectively, in an Ethiopian study,*(18)* demonstrating that the equation used to calculate eGFR may also explain variations in prevalence. Two studies on patients with type 1 and type 2 diabetes were conducted in two different places in Tanzania. Janmohamed et al, found 79.9% had albuminuria and 83.7% had CKD (eGFR<60 ml/minute/1.73m^2), *(19)* while in Lutale et al, 17% had albuminuria and 22% had CKD stages 3 to 5. *(20)* Their methods of determining proteinuria and target populations varied in ages, duration of diabetes and other characteristics. The prevalence of CKD in

studies in sub-Saharan Africa is relatively high, in spite of the differences in patient characteristics within diabetes and the methods used to determine the eGFR. However, CKD and albuminuria still exhibit common determinants of aging, hypertension, poor glycaemic control and socio-economic challenges where they were evaluated. This study did not show glycaemic control as a significant predictor of chronic kidney disease.

Screening and case finding for CKD in patients with diabetes is important because early stage disease can be managed to delay progression. *(21, 22)*

The potential cost of morbidity and mortality from progressive CKD in type 2 diabetes is enormous, barely affordable in resource-scarce settings. This is much more important in high-risk individuals where the factors that initiate CKD are often the drivers of CKD progression.

Renal functions do improve when therapeutic targets are attained, *(23)* therefore CKD and its drivers of progressions should be actively sought for in patients attending general diabetes clinics as standard of care. Modelling of data on screening strategies has demonstrated the cost-effectiveness of screening for CKD and optimally managing hypertension. *(24)*

Our study showed that age above 50 years, (and age as a continuous variable), was associated with having CKD/KDIGO stages 3 to 5. In addition, living with diabetes for 5 years and more, increased the odds of having advanced CKD stages. Similarly, other studies have demonstrated that aging is associated with deteriorating kidney function *(25, 26),* and long duration of diabetes compounds it. *(27)* These parameters are easily determined in clinics and should assist in stratifying our patients into risk categories during routine follow-up for case-finding, especially in patients who also have other risk factors like hypertension, chronic poor glycaemic control and cigarette-smoking.

Hypertension, a modifiable risk factor increased by 3-fold, the odds of having advanced CKD stages in this study. Hypertension causes chronic kidney disease in type 2 diabetes *(28, 29, 30, 31, 32)* and other cardiovascular events like heart failure *(33)* and stroke *(34, 35)* but when hypertension is under control in such subjects who retain normal kidney function, it mitigates the potential for developing CKD. *(36, 37)* Conversely, poor or insufficient control of hypertension initiates CKD (and causes progression of CKD to more advanced stages). Use of ACEi's/ARB's in control of hypertension mitigates renal disease progression. *(38, 39, 40, 41)* Our study registered 69.0% users of ACEi/ARB agents; however, we did not determine duration of use, doses nor the adherence patterns. Just below a quarter of our study patients with hypertension, at the time of enrolment, had optimal control of the high blood pressure. We have previously documented similar modest proportion of patients with hypertension on type 2 diabetes who achieved optimal Blood Pressure control while on treatment. *(42)* Another study elsewhere in sub-Saharan Africa *(43)* also reported similar small proportions.

From this study we infer that diabetes care in the clinic was neither sufficient to achieve optimal control of the modifiable risk factors nor able to detect complications in the patients. These findings suggest that patients, with type 2 diabetes for 5-years and more, aged 50 years and above, have hypertension, are

cigarette-smokers and of modest socio-economic capacity should be screened for CKD. Many patients with type 2 diabetes who attend public hospital clinics in sub-Saharan Africa, may look well, but they will need screening for CKD. The WHO document of Wilson and Jungner *(44)* support CKD screening amongst patients with type 2 diabetes because it is a public health problem, early disease is recognizable, screening tests are acceptable to populations, amongst its ten items. Indeed, screening for chronic kidney disease in diabetes has been recommended but in the developed world *(45, 46, 47).* A review from experts to justify the same for overall CKD screen in sub-Saharan Africa was recently published.Screening for a disease demands availability of (or access to) treatment and that is our major undoing in sub-Saharan Africa. *(48, 49)* Improved public health systems, however should equalize opportunities for access to quality care, in this context, of high-risk diabetic patients like these in our study. The audit part of this study has been published *(50).* However, that spot urine test for albuminuria and occasional kidney function test for eGFR are not often done on these patients, as standard of care, this unmasked the clinical information missed out if these tests were done deliberately.

Conclusions

Screening for CKD and case-finding without linkage to clinical care for control of risk factors and its management is an exercise in futility.

Therefore, governments must endeavor to enable public health systems or hospitals to improve the quality of diabetes care they offer. This includes enhancing the level of clinical care, deliberately screening for and case-finding of chronic kidney disease and then link, provide and retain them in appropriate care that should consequently forestall the more costly ESRD or cardiovascular events and/or mortality.

Abbreviations

CKD - Chronic Kidney Disease, *KDIGO* - Kidney Disease. Improving Global Outcomes. *ACEi/ARBs*- Angiotensin Converting Enzyme inhibitors/Angiotensin Receptor Blockers.

Declarations

Ethics approval and consent to participate. The studywas duly approved by the ERC of University of Nairobi/Kenyatta National Hospitaland that of Nyeri County Referral Hospital, and its publication was expected.Each participatingpatient received full explanation of the study and voluntarily gave informed consent to participate, and the results obtained informed the care offered.

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Author contributions OCF: design of the study, wrote all the drafts, and the final manuscript. MWK: design of study, data collection, read the drafts, and made inputs in the manuscript. OEN: design of study, read the drafts, and made critical input into the final manuscript. MK: participated in the design, sample size calculation, and statistical analysis. All authors contributed towards data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

*Competing interest.*We as the authors of this manuscript declare that there are no special interests served by this publication except for academic information.

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Tables

Table1: Clinical and laboratory characteristics by gender of the study patients.

Variable	Overall(N=385) N (%)	Female(N=252) N (%)	Male (N=133) N (%)	OR (95% CI)	P value
Age, years, mean(SD)	63.3	62.1(12.0)	65.7(13.7)	-	**0.006**
BMI,kg/m^2,mean (SD)	26.7 (4.6)				
Categories, n (%)					
Underweight- (<18.5kg/m^2)	6 (1.6)	4 (1.6)	2 (1.5)	1.5 (0.3-	0.660
Normal- (18.5-25kg/m^2)	139 (36.1)	80 (31.7)	59 (44.4)	8.3)	-
Overweight- (25-29.9kg/m^2)	154 (40.0)	102 (40.5)	52 (39.1)	1.0	0.127
Obese- (≥30kg/m^2)	86 (22.3)	66 (26.2)	20 (15.0)	1.4 (0.9-	**0.004**
				2.3)	
				2.4 (1.3-	
				4.4)	
Waist Circumference, cm, mean (SD)	92.5 (22.0)				
Categories, n (%)	224 (58.2)	171 (67.9)	53 (39.8)	3.2 (2.1-	**<0.001**
Undesirable, >102cm(M)/>88cm(F)	161 (41.8)	81 (32.1)	80 (60.2)	4.9)	
Normal				1.0	
				-	
Hypertension, BP>140/90mmHg					
Hypertensive, n (%)	191 (49.6)	196(77.8)	99 (74.4)	1.2 (0.7-	0.461
Normal BP	194 (50.4)	56 (22.2)	34 (25.6)	2.0)	
				1.0	
Glycemic control, HbA1c (%)					
Glycaemia, HbA1c %, mean(SD)	8.1(2.8)	8.3(3.0)	7.9(2.7)	-	0.181
Poor control, HbA1c >7.0	233(60.5)	154(61.1)	79(59.4)	1.1(0.7-	0.744
Optimal control, HbA1c ≤7.0	152(39.5)	98(38.9)	54(40.6)	1.6)	
				1.0	
Total cholesterol, mean (SD),mmol/L	4.6 (1.2)	4.9(1.2)	4.2(1.1)	-	**<0.001**
Categories, n (%)					
	88 (22.9)	69 (27.4)	19 (14.3)	2.3 (1.3-	**0.004**
High>4.120	297 (77.1)	183 (72.6)	114 (85.7)	4.0)	
Optimal≤4.120				1.0	
HDL-cholesterol, mean (SD),mmol/L	1.3 (0.9)	1.4(0.3)	1.3(1.5)	-	0.719
Categories, n (%)					
	80 (20.8)	39 (15.5)	41 (30.8)	0.4 (0.2-	**<0.001**
Low≤1.0	305 (79.2)	213 (84.5)	92 (69.2)	0.7)	
Optimal>1.0				1.0	
Triglycerides, mean (SD), mmol/L	1.7 (1.0)	1.7(1.0)	1.7(1.1)	-	0.873
Categories, n (%)	210 (54.5)	135 (53.6)	75 (56.4)	0.9 (0.6-	0.597
High >1.7	175 (45.5)	117 (46.4)	58 (43.6)	1.4)	
Optimal≤1.7				1.0	
LDL-cholesterol, mean(SD, mmol/L	2.4 (0.9)	2.6(0.9)	2.2(0.9)	-	**<0.001**

Categories, n (%) High>2.0 Optimal≤2.0	297 (77.1) 88 (22.9)	206 (81.7) 46 (18.3)	91 (68.4) 42 (31.6)	2.1 (1.3-3.4) 1.0	**0.003**
CKD/(KDIGO categories) **G1, eGFR>90ml/min/m^2** **G2, eGFR 60-90** **G3a eGFR 59-45** **G3b eGFR 44-30** **G4 eGFR 29-15** **G5 eGFR<15**	 77 (20.0) 158 (41.0) 81 (21.0) 48 (12.5) 18 (4.7) 3 (0.8)	 53 (21.0) 106 (42.1) 48 (19.0) 30 (11.9) 13 (5.2) 2 (0.8)	 24 (18.0) 52 (39.1) 33 (24.8) 18 (13.5) 5 (3.8) 1 (0.8)	 1.0 0.9 (0.5-1.7) 0.7 (0.3-1.3) 0.8 (0.4-1.6) 1.2 (0.4-3.7) 0.9 (0.1-10.5)	 0.789 0.211 0.467 0.779 0.937
Albuminuria status Albuminuria present NO Albuminuria	 126 (32.7) 259 (67.3)	 80 (31.7) 172 (68.3)	 46 (34.6) 87 (65.4)	 0.9 (0.6-1.4) 1.0	 0.572

Table 2: Treatment Information of the study patients

Variable	Proportion, N (%)
Diabetes mellitus treatment	
Diet-only	11 (2.9)
Oral Glucose-lowering Agents(OGLAs)-only	262 (68.1)
Insulin-only	66 (17.1)
Insulin combined with Oral Glucose-lowering Agents	46 (12.0)
Other co-medications used regularly by the subjects	
Anti-platelets	45 (11.7)
Statins	48 (12.5)
Anti-platelets and statins	108 (28.1)
Anti-hypertensive drugs	295(76.6)
- ACEi/ARBs	204(69.0)
Frequency of clinic attendance in the last 12 months	
2 - 3	68(17.7)
4 - 5	292(75.9)
6 and above	25 (6.5)

ACEi – Angiotensin Converting Enzyme inhibitors, ARBs – Angiotensin Receptor Blockers.

Table 3: Bivariate analysis of factors associated with Chronic Kidney Disease in the study subjects.

Variable	Chronic Kidney Disease, CKD /KDIGO classification		OR (95% CI)	P value
	Stage 3-5	Stage 1-2		
Age, mean (SD), years	70.8 (8.8)	58.6 (11.5)	-	**<0.001**
Age category, years				
≤50	0 (0.0%)	54 (100.0%)	-	**<0.001**
>50	150 (45.3%)	181 (54.7%)		
Gender				
Female	93 (36.9)	159 (63.1)	0.8 (0.5-1.2)	0.255
Male	57 (42.9)	76 (57.1)	1.0	
Marital status				
Single, unmarried	2 (9.1)	20 (90.9)	1.0	
Married.	96 (37.2)	162 (62.8)	5.9 (1.4-25.9)	**0.018**
Widowed	52 (51.0)	50 (49.0)	10.4 (2.3-46.8)	**0.002**
Separated	0 (0.0)	3 (100.0)	-	0.999
Level of formal education				
None	29 (56.9)	22 (43.1)	1.0	
Primary school(1-7yrs)	87 (38.3)	140 (61.7)	0.5 (0.3-0.9)	**0.017**
Secondary school(8-12yrs)	26 (28.9)	64 (71.1)	0.3 (0.2-0.6)	**0.001**
Tertiary, >12yrs in school	8 (47.1)	9 (52.9)	0.7 (0.2-2.0)	0.483
Employment status				
Unemployed	56 (44.8)	69 (55.2)	1.0	
Employed	3 (13.0)	20 (87.0)	0.2 (0.1-0.7)	**0.009**
Self-employed	47 (31.5)	102 (68.5)	0.6 (0.3-0.9)	**0.025**
Retired	44 (50.0)	44 (50.0)	1.2 (0.7-2.1)	0.454
Cigarette smoking				
Smoker	38 (41.3%)	54 (58.7%)	1.1 (0.7-1.8)	0.597
Non-smoker	112 (38.2%)	181 (61.8%)	1.0	
Duration of diabetes, years, median (IQR)	11.0 (5.0-18.0)	5.0 (2.0-11.0)	-	**<0.001**
Duration of disease, categories, years				
>5	105 (48.2%)	113 (51.8%)	2.6 (1.7-4.1)	**<0.001**
≤5	41 (26.1%)	116 (73.9%)	1.0	
LDL-cholesterol, mmol/L				
High>2.0	116 (39.1)	181 (60.9)	1.0 (0.6-1.7)	0.943
Normal ≤2.0	34 (38.6)	54 (61.4)	1.0	
Obesity				
Obese, BMI ≥30 **kg/m^2**	17 (19.8)	69 (80.2)		**<0.001**

Not obese, BMI <30 kg/m^2	133 (44.5)	166 (55.5)	0.3 (0.2-0.5) 1.0	
Hypertension, BP>140/90mmHg Hypertensive Normal BP	 91 (47.6) 59 (30.4)	 100 (52.4) 135 (69.6)	 2.1 (1.4-3.2) 1.0	**0.001**
Systolic BP,mean (SD) mmHg	148.8 (25.6)	140.3 (20.6)	-	**<0.001**
Diastolic BP,mean (SD) mmHg	81.9 (12.1)	81.2 (10.9)	-	0.579
Glycemic control Poor (HbA1c>7.0%) Good (HbA1c≤7.0%)	 86 (36.9) 64 (42.1)	 147 (63.1) 88 (57.9)	 0.8 (0.5-1.2) 1.0	0.307

Table 4: Logistic regression model of the Predictors of Chronic Kidney Disease (CKD) in the study subjects.

Variable	Adjusted Odds Ratios			p- value
	Odds Ratio	95% C.I.		
		Lower	Upper	
Age, above 50 years	1.12	1.09	1.16	**<0.001**
Duration of diabetes (>5 years) Duration of diabetes, years	1.98 1.05	1.17 1.05	3.36 1.08	**0.012** **0.005**
Obesity, BMI ≥30 kg/m^2	0.24	0.12	0.47	**<0.001**
Systolic Blood Pressure, SBP≥140mmHg Hypertension present	1.014 2.3	1.003 1.2	1.025 4.5	**0.012** **0.015**

Table 5: Logistic regression of Risk factors and loading on patients with Chronic Kidney Disease in the study.

Variable	Chronic Kidney Disease (CKD)	Normal, non-CKD	OR (95% CI)	P value
Risk factor loading,				
0-Normal Blood Pressure	20 (22.2%)	70 (77.8%)	1.0	
1-Hypertension (HTN)	53 (47.3%)	59 (52.7%)	3.1 (1.7-5.8)	**<0.001***
2-HTN+HbA1c>7.0%	20 (42.6%)	27 (57.4%)	2.6 (1.2-5.6)	**0.014***
3-HTN+HbA1c+LDL>2.0mmol/L	0 (0.0%)	13 (100.0%)	-	0.999
4-HTN+A1c+LDL+Age+Dur<5yr	17 (34.7%)	32 (65.3%)	1.9 (0.9-4.0)	0.114
5-HTN+HbA1c+LDL+Age+Dur≥5yr	29 (50.9%)	28 (49.1%)	3.6 (1.8-7.4)	**<0.001***
6-HTN+A1c+LDL+Age+Dur>5yr+Cig	11 (64.7%)	6 (35.3%)	6.4 (2.1-19.5)	**0.001***
7- **ACEI/ARB-use**	111 (41.6)	156 (58.4)	1.4 (0.9-2.3)	0.114
Yes	39 (33.1)	79 (66.9)	1.0	
No				

CKD=Chronic kidney disease, stages 3 to 5, Age = Age>50 years, Dur = Duration of diabetes, Cig = Cigarette-smoking, HTN=Hypertension, LDL = Low Density Lipoprotein Cholesterol.

Figures

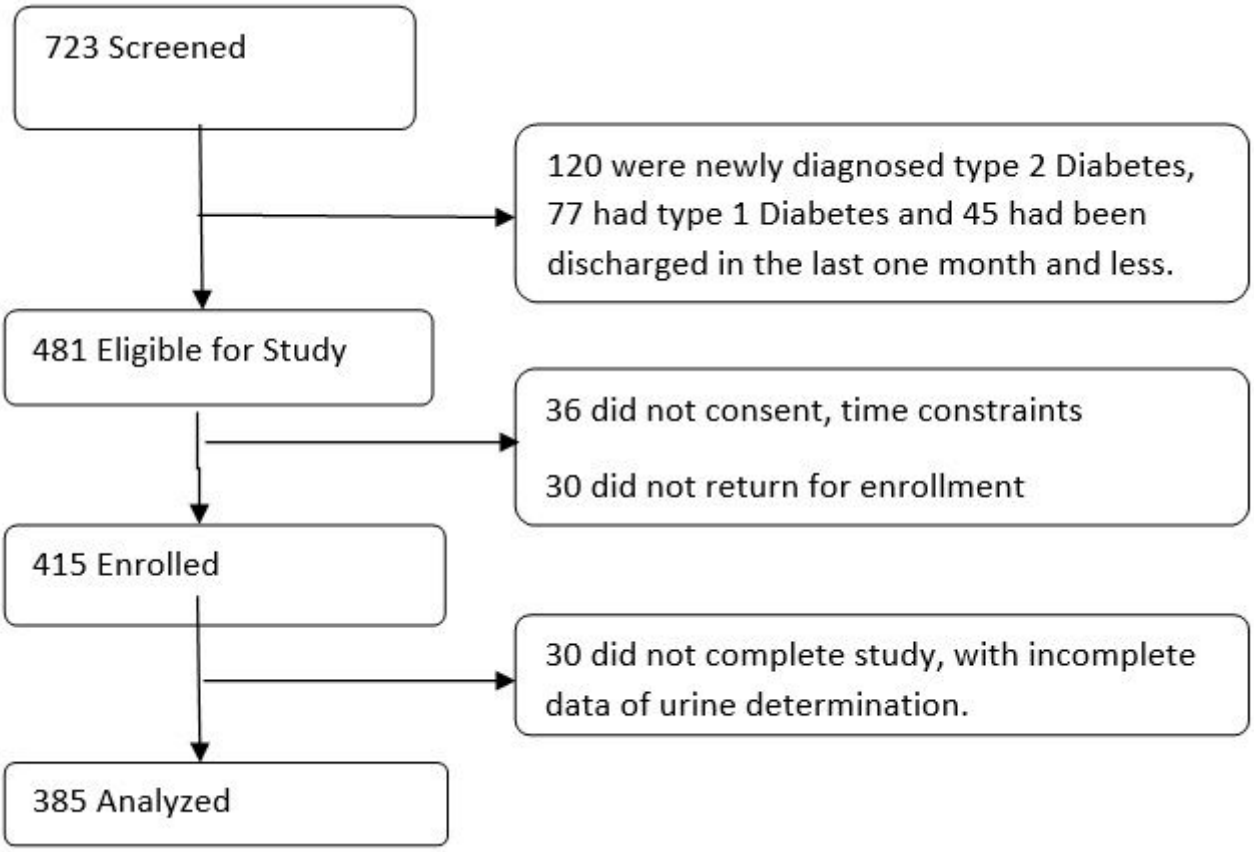

Figure 1

A flow chart of recruitment and enrolment of subjects into the study.

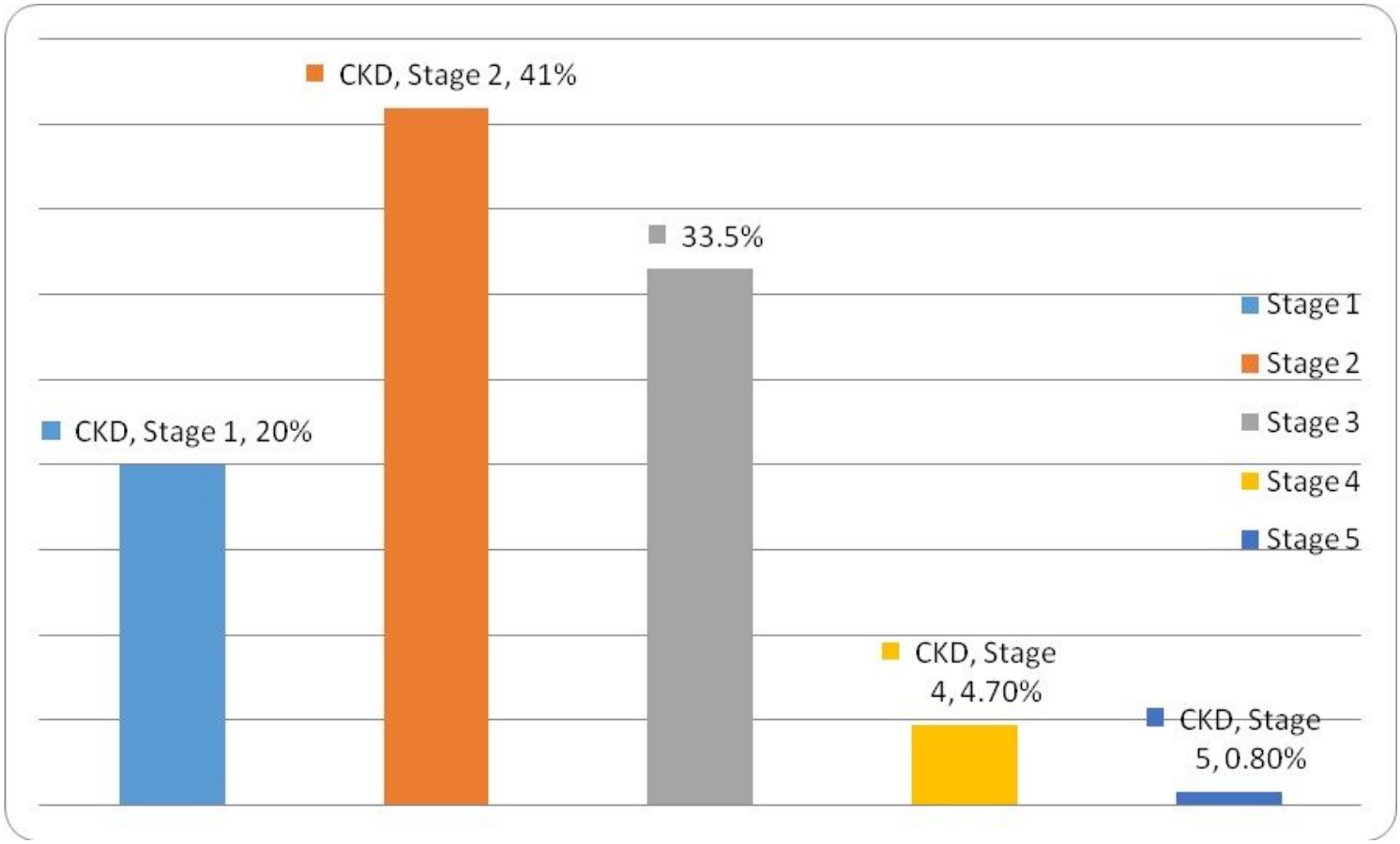

Figure 2

Figure 2: Chronic Kidney Disease/KDIGO stages and the proportions of study subjects in each stage.

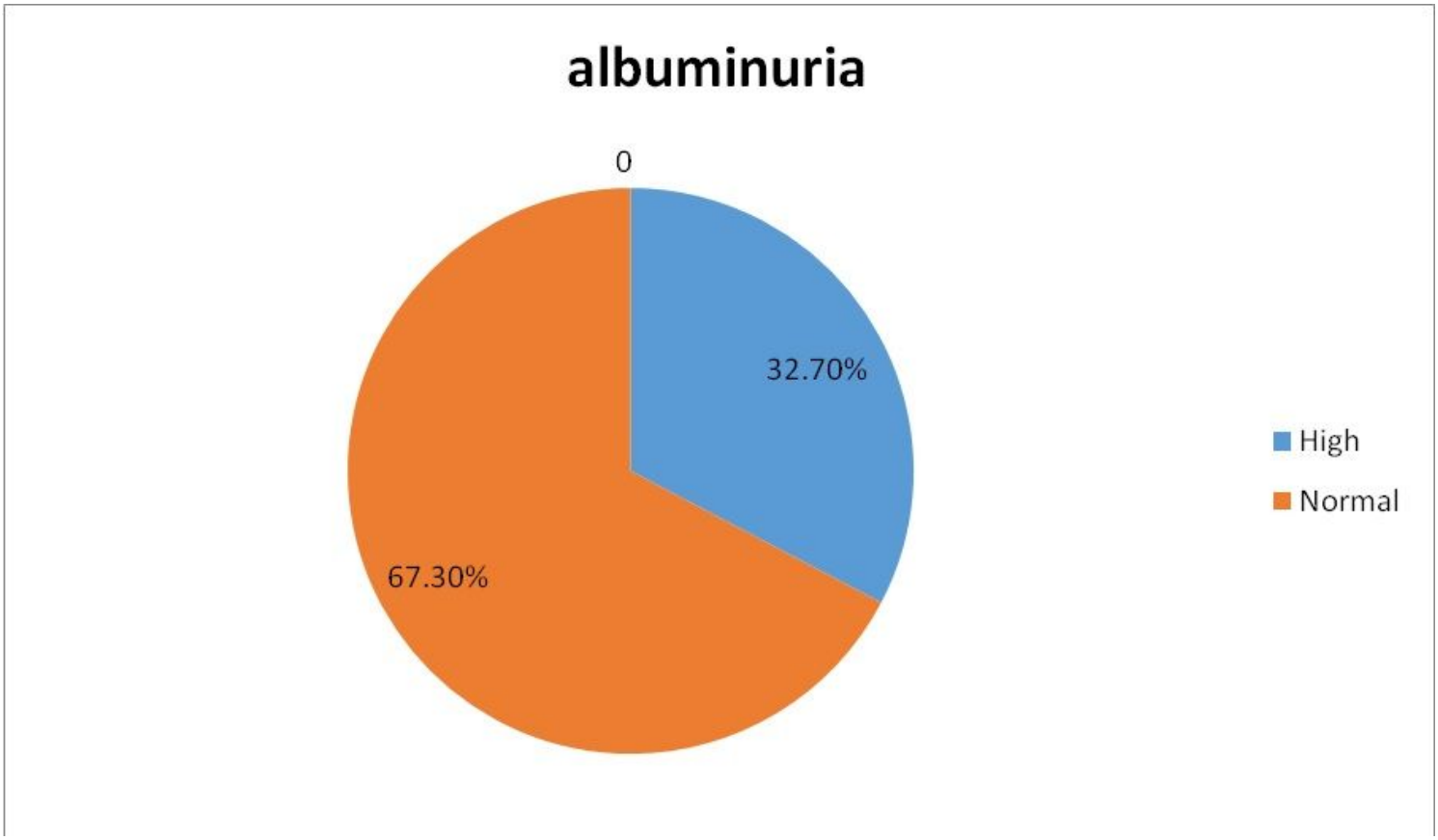

Figure 3

Figure 2: Albuminuria status of the study subjects.