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CHRONIC KIDNEY DISEASE AMONG TYPE 2 DIABETIC PATIENTS ATTENDING DIABETIC CLINICS IN JIGAWA, NIGERIA

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Abstract

Chronic kidney disease (CKD) among diabetic patients develops cardiovascular abnormalities with increased morbidity and mortality risk. CKD is commonly seen among elderly, some ethnic groups and disadvantaged populations which were identified with increased type 2 DM prevalence and its burden/complications with non-equitable access to renal replacement therapies. The study aimed to determine the prevalence of CKD among diabetic patients and to assess risk factors specific to zonal areas in the state. A total of 130 diabetic patients attending clinic and 100 controls were recruited. Patients and controls were assessed for blood pressure (BP), body mass index (BMI), albumin-to-creatinine ratio (ACR), serum and urinary creatinine, urinary albumin, glycaeted haemoglobin and fasting blood glucose. CJD, as defined

[redacted]

KEYWORDS:
Chronic kidney disease, Albumin Creatinine Ratio (ACR), Poverty, Glycemic index foods (FGI), senatorial zones

by ACR ranges from A1 (ACR < 3 mg/mmol) to A3 (> 30 mg/mmol). Of the 130 patients, 20% were having CKD. Patients with 0-5 years duration of diagnosis had CKD prevalence of 25%, 6-7 years had 37%, while >10 yrs had 50%. Poor glycaemic control had CKD prevalence of 27%, borderline 18% and good glycaemic control had 9%. North east zone had (26%) while North-West and South-West groups were having 17% and 18% respectively. Female had 21% compared to male (19%). Poverty distribution is 79% among patients with diabetic only, 67% in controls and 92% in patients' with both DM and CKD. High and low glycemic index foods were 80/20% and 93/7% among patients and controls respectively. Other related risk factors were age and inappropriate use of agro-chemicals in some areas. Routine kidney assessment and improved policy on use of agrochemicals should be addressed.

Introduction

Chronic kidney disease (CKD) has deleterious effect on kidney structure and function. It is clinically defined as the presence of microalbuminuria or overt nephropathy in patients with diabetes who lack indicators of other renal diseases (IDF, 2017; Moleife-Baiki, *et al*., 2018; Umanatha and Lewis, 2018). KDIGO (2013) expressed chronic kidney disease as "abnormalities of kidney structure or function, present for more than 3 months, with implications for health".

Like other micro-vascular complications, the pathogenesis of diabetic nephropathy is related to chronic hyperglycaemia. Other risk factors associated with the development of microalbuminuria include duration of diabetes, family history of vascular complication, obesity, higher blood pressure, higher blood glucose level, dyslipidaemia and smoking among others (Hovind *et al*, 2004; ADA, 2018).

However, persons with Type 2 diabetes exhibit the highest prevalence; particularly African-American, native American, Asian and Hispanic were also at higher risk of end stage renal disease (ESRD) than non-Hispanic white persons (Parving *et al.,* 2006). Diabetic nephropathy may progress from microalbuminuria to macroalbuminuria with progressive loss of glomerular filtration rate (GFR) until ESRD (Alicic *et al*., 2017).

In sub-Saharan Africa, chronic kidney disease (CKD) has been documented with high prevalence across the region, with both communicable and non-communicable as risk factors (Abd-ELHafeez *et al*., 2016). This may not be unconnected with some factors including changing lifestyle, poverty, urbanization and globalization (Noubiap *et al*., 2015), delayed diagnosis and treatment and unregulated use of agrochemicals by farmers.

A high prevalence of CKD has also been reported in rural agricultural communities in developing countries. The strong association with farm work has led to suggestions that exposure to agrochemicals, dehydration and consumption of contaminated water might be responsible (Almaguer *et al*., 2014; Li *et al*., 2015). Exposure to pesticides may produce biochemical changes even before the clinical health manifestation that may appear in the handlers' results from destructive and degenerative changes in many organs including kidneys (Khan *et al*., 2013). Various studies have shown that farm workers exposed to pesticide showed significant increase in serum level of urea and creatinine (Yassin and Al-shanti, 2016) as markers for kidney injury.

Dialysis and renal transplantation are costly and can have a devastating effect on quality and length of life (Goldschmid *et al*., 1995; ADA, 2018). It has become clear over time that once overt nephropathy has developed, treatment is a delaying rather than a preventive tactic. Therefore, health plans should be aimed at managing CKD epidemics in Africa. This could be achievable through substantial articulation on a reliable assessment with established and affordable early detection programs as contained in the World Health Assembly target to reduce premature mortality from chronic diseases by 25% in 2025 (Abd-ELHafeez *et al*., 2016). Assessment of renal function is therefore imperative, as early diagnosis of CKD may suggest early therapeutic interventions in preventing or delaying the onset of later complications with possible improvement of outcomes (Gheith *et al*., 2014). It may also reveal the current happening in the environment on handling agrochemicals and how injurious they are to the public health.

MATERIALS AND METHODS

Jigawa State is located in North West part of Nigeria, bordered by Kano, Katsina, Yobe and Bauchi States as well as Niger republic. Rasheed Shekoni specialist hospital is situated in Dutse, the state capital, provides diagnosis, treatment and other health care services at tertiary level to patients.

Approval for the study was obtained from the Research Ethical Committee of Jigawa State ministry of health and Rasheed Shekoni specialist hospital. An informed written and verbal consent was obtained from all participants. Patients with pregnancy, hypertension, acute illness, hospitalization, fever, strenuous exercise, non-fasting, on dialysis and other possible causes to increase or affect the level of microalbuminuria were excluded.

A total of 130 participants regularly attending their clinic were recruited in the study. Fasting blood samples were taken for the assessment of FBG, MDA, both serum and urinary creatinine (SCr and UCr respectively) and lipid profile were assessed spectrophotometrically. GHbA1c was measured using chromatographic method while ACR was evaluated and repeated three (3) times at an interval of 1month within 3 months duration for persistent microalbuminuria adopting immuno-turbidimetric method. Glucose, GHbA1c, MDA and ACR were measured immediately while the remaining sera and urine were kept frozen at -20°C for two weeks prior to analysis.

Demographic information was collected during the visit. Other variables including weight (kg) was taken in light clothes and without shoes and height (meters) measured without shoes and were used for the calculation of body mass index (BMI). Blood pressure was measured using a mercury sphygmomanometer in the sitting position at triaging cubicle. In this study, hypertension was defined as systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg or use of any form of antihypertensive medication.

RESULTS

A total of 130 (68 males and 62 females) type 2 diabetic and non-hypertensive patients were recruited at the initial stage of the study. Ethnicity was dominated by Hausa with 103 (79%) followed by Fulani 20 (15%) and Kanuri 7 (5%) of the total population. On the marital status, married have 118 (91%), bachelors 7 (5%) and widow 5 (4%). Family history of diabetes mellitus (FHDM) 75 (58%) have the history, while 55 (42%) has no history. History of hypertension (FHH) indicated 41 (32%) with positive history and

89 (69%) have no history or not aware. Family history of obesity (FHO) was also assessed of which 30 (23%) have answered yes, while the remaining 100 patients (76%) said no. Additionally, smoking was indicated in only 5 (4%) but all seized smoking for the last one year as presented in Table 1.

According to Table 2, the clinical and anthropometric variables including BMI, WC and SBP were significantly higher among patients than controls ($p<0.05$) except DBP which was silent statistically.

With respect to Table 3, the biochemical parameters assessed tends to be raised significantly in patients than controls. This include SCr, GHbA1c, ACR, MDA, FBG, TC, LDL-C and TC/HDL-C ratio ($p<0.05$). UCr and TG although higher in patients but were insignificant accordingly. On the other hand, HDL-C was significantly lower in patients compared to the controls ($p<0.000$).

From the 130 diabetic patients, the prevalence of CKD was 26 (20%) while 104 (80) were normo-albuminuric. The prevalence based on DOD, patient with 0-5 years have the least prevalence of 25% followed by patients group with 6-7 years having 37%. Patients of greater than 10 years (>10 yrs) DOD has the highest prevalence of 50% compared to other groups.

According to the glycaemic control status poor glycaemic control have the highest prevalence of 27%, borderline glycaemic control group with 18% and followed lastly by good glycaemic control group with only 9%.

The results according to senatorial zones has shown that the prevalence of microalbuminuria was higher (26%) in the North East zone while North-West and South-West groups were having the prevalence's of 17% and 18% respectively as presented in Figure 1.

According to gender, the results revealed that prevalence of microalbuminuria among female was higher (21%) among female patients when compared to the male (19%).

Of the 130 diabetic patients recruited, 104 (80%) of the patients with diabetes mellitus in the locality depend on foods with higher glycaemic index compared with those on low glycaemic index food with only 26 (20%) proportion from Table 1.

According to Figure 2, poverty distribution among the participants recruited is 79% (103). Patients' having both DM and CKD the percentage distribution of poverty among them is 92% (26). Participants serving as controls with100 apparently healthy individuals had only 67% proportion with poverty.

Table 1: Socio-Demographic Characteristics of the Study Participants

Variables	Yes n(%)	No n(%)
FHDM	75 (57.7)	55 (42.3)
FHHTH	41 (31.5)	89 (68.5)
FHO	30 (23.1)	100 (76.9)
SMOKING	5 (3.8)	125 (96.2)
FGI		
High	104 (80)	
Low	26 (20)	

Key: n=population, size **FGI=**Food glycaemic index, FHO=Family history of Obesity, FHHTN=Family History of Hypertension, FHDM=Family History of Diabetes

Table 2: Clinical and Anthropometric Parameters in Normo-tensive Type 2 Diabetes Patients and Controls

Variables	Patients Mean±SD	Control Mean±SD	p-value
Height	1.64±0.09	1.66±0.08	**0.012***
Weight	68.19±15.39	64.49±10.44	**0.040***
BMI	25.02±5.93	23.41±4.32	**0.023***
WC	87.13±9.44	82.16±14.10	**0.002***
DBP	73.19±8.45	72.71±6.85	0.642
SBP	114.96±10.27	117.61±7.34	**0.030***

Key: BMI-body mass index; WC-waist circumference; DBP-diastolic blood pressure; SBP-systolic blood pressure

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Table 3: Biochemical Parameter in Type 2 Diabetes Patients and Controls

Variables	Patients Mean±SD	Control Mean±SD	p-value
S-Creatinine (μmol/L)	100.04±21.01	78.88±14.16	**0.006***
U-Creatinine (μmol/L)	9598.82±4926.51	8495.27±1913.75	**0.035***
ACR mg/mol	16.73±12.10	0.9604±0.41	**0.000***
MDA mmol/L	13.99±2.94	8.23±1.96	**0.000***
FBG mmol/L	6.26±2.83	3.50±0.70	**0.000***
GHbA1c %	8.39±8.94	4.91±0.74	**0.000***
T-C mmol/L	3.36±0.52	3.13±0.34	**0.000***
HDL-C mmol/L	1.25±0.33	1.65±0.39	**0.000***
TG mmol/L	0.78±0.27	0.75±0.29	0.371
LDL-C mmol/L	1.76±0.41	1.19±0.30	**0.000***
TC/HDL-C-ratio	2.82±0.64	1.98±0.51	**0.000***

Key: *=significant SD=standard deviation; ACR-albumin-creatinine ratio; MDA-malondialdehyde; FBG-fasting blood glucose; T-C-total cholesterol; HDL-C high density lipoprotein-cholesterol; LDL-C- low density lipoprotein-cholesterol; TC/HDL-C-ratio- iatrogenic index

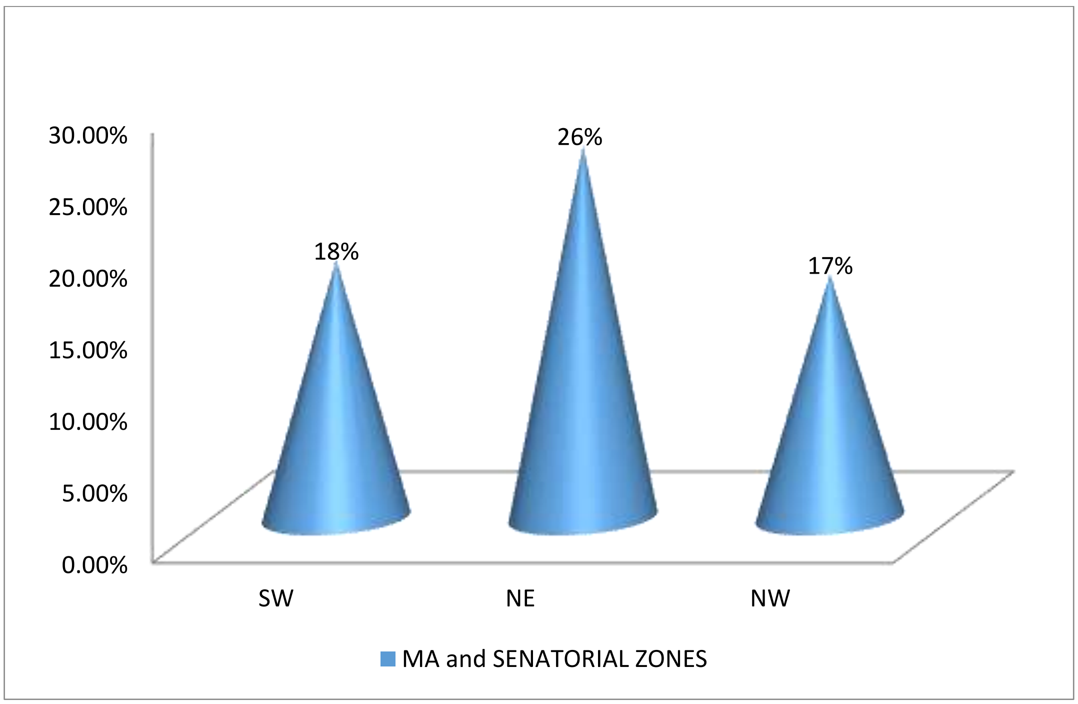

Fig. 1 Prevalence of microalbuminuria among diabetic patients from different senatorial zones

Key- MA = microalbuminuria, SW = South-West, NE = North-East, NW = North-West

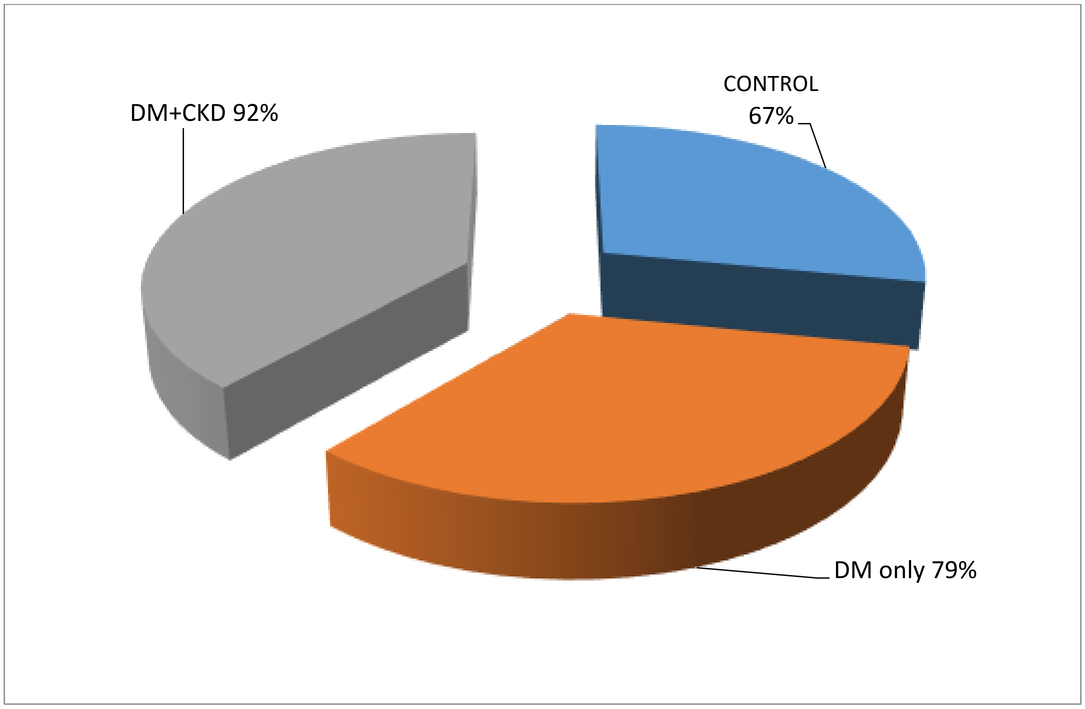

Fig. 2 Poverty among patients with diabetes mellitus and controls
MA = microalbuminuria, DM = diabetes mellitus, DM+CKD = diabetes mellitus plus chronic kidney disease

STATISTICS

The data was entered in to excel sheets and the analysis was made using SPSS statistical software, version 20.0. The outcomes were expressed as mean (SD) and statistically significant when $p<0.05$. Independent-student's *t*-test was employed for comparison of variables between patients and controls participants.

DISCUSSION

Diabetes mellitus (DM) is a common metabolic condition worldwide. Among its striking complications is chronic kidney disease (CKD) which is the primary cause of end-stage renal disease aetiology (Parving *et al*., 2006; ADA, 2018).

Twenty percent (20%) was determined as the prevalence of diabetic nephropathy among DM patients in Jigawa State, Nigeria. The presented prevalence value implies that in every 10 diabetic patients in Jigawa, 2 are having or will develop renal complication. This is a very significant number in a population with limited access to standard medical care coupled with poverty as the case in Jigawa (Ajibola and Sanni, 2015; NHDR, 2018). New *et al*. (2007) showed that patients with diabetes were seven times more likely to have clinically significant CKD compared to those without diabetes.

The prevalence of the study closely agreed with the findings in Zaria by Ahmad *et al.* (2014) reported 23%. The prevalence falls within the range reported by Noubiap *et al.* (2015) in sub-Saharan Africa from 4 to 24% based essentially on proteinuria defined CKD. The result also agreed to the Caucasians reports on Type 2 diabetic patients with prevalence of 20% by Torffvitt *et al.* (1991) and 21% by Khikhava *et al*. (1989). Ethnicity in relation to CKD development is not well defined in our community. Black ethnic group may have similar prevalence rates of CKD with white population, but tend be at higher risk of progressive and adverse renal events due to genetic or other confounding factors including socioeconomic status and reduced accessibility to healthcare facilities (Robbings *et al.,*.2001; Hsu *et al*., 2003).

The reported prevalence in this study was much lower when compared to some local findings here in Nigeria as reported by Iwalokun *et al.* (2006) with prevalence of 37.6%, 50% in Benin by Unuigbe *et al.* (2001) and 52% by Erasmus *et al.* (1992) in Ilorin. The most likely reason for the disparity in the prevalence between the present study and other studies was the used of MICRAL strip or CLINITEK a semi-quantitative ACR test for urinary albumin assessment which has been reported to be less specific than the Immuno-turbidimetric method (Lutale *et al*., 2007) employed in the present study. Low quality researches were identified by Noubiap *et al.* (2015) where much higher prevalence of CKD among African ranges between 21% and 45% was reported, regardless of the definition. Another possible reason for the differences between the studies may be patients' population size, experimental design and most likely methods for collection of urine and assessment of microalbuminuria also suggested by Molefe-Baikai *et al*. (2018).

The study observed that constrains facing the diagnosis of CKD in Africans are commonly related to availability and accessibility of screening or diagnostic tools. A review by Swanepoel *et al*. (2013) has pointed out lack of amenities among other problems associated with nephrology in Africa in diagnosing renal diseases. Also, the study found no recordings of SCr for 87% and a record of albuminuria testing for only 7%, indicating that monitoring of renal function is suboptimal in this area. The current finding on CKD prevalence among the diabetic patients therefore confirms the need to strategize tools in monitoring renal function effectively.

Considering the patients based on glycaemic status, duration of disease (DOD), gender and senatorial zones, the respective prevalence's were found to differ considerably. As one of the major determinant of micro-vascular complications, the present study, based on the glycaemic control, has suggested that an increase in GHbA1c increases the risk of developing microalbuminuria over some time. Participants were redistributed according to good control, borderline and poor glycaemic control status. The groups therefore were found to have a simultaneous linear increase between GHbA1c status and microalbuminuria as the control worsens. This signified the clinical usefulness of GHbA1c assay in evaluating glycaemic control among diabetic patients in this environment. Therefore, GHbA1c is a strong risk factor associated with progression of microalbuminuria and that controlling hyperglycaemia will lead to halting or slowing the progression of diabetic nephropathy to end stage renal disease (DCCT, 1993). The strong influence it has on both MDA and ACR as shown in this study further confirmed its utility in prognosis of the disease. In contrast, most of the available studies from sub-Saharan African (Lutale *et al*., 2007) fail to demonstrate any significant relationship between the level of glycaemic control and microalbuminuria. It has been observed that 0.5% decrease in GHbA1c is clinically significant and comparable to what could be achieved using medication in newly diagnosed Type 2 DM (UKPDs, 1998). Reduction by 1% of GHbA1c as reported by UK-PDSG was associated with a reduction in risk of 21% (95% CI, p <0.0001) and a reduction in risk of 37% (95% CI, p < 0.0001) for micro-vascular complications and that any reduction in glycaeted haemoglobin is likely to reduce the risk of complications (UKPDs, 1998; UKPDs, 2000).

Regarding to the categorization based on DOD, the present study revealed that the prevalence of microalbuminuria tends to increase with duration of the disease. The linear association observed in this study agrees with the relative finding of Lutale *et al*. (2007) in Tanzania and Iwalokun *et al.* (2006) in Lagos where they observed a linear relation between duration of diabetes and the incidence of microalbuminuria. Duration of diabetic diagnosis (DOD) has been identified as non-modifiable risk factor (Ahmad *et al*., 2014) in the development of microalbuminuria in diabetic nephropathy especially where poverty, lack of proper diagnostic tools and drug accessibility prevails. In addition to the warring up of normal body function with increase in hyperglycaemia generated ROS and low nutrients supply to the system, deterioration and DM related complications are likely to descend (Azab *et al*., 2017). Report from ADA (2018) stated that duration of glycaemic burden is a strong predictor of adverse outcomes associated with DM.

According to senatorial zones in Jigawa State, the study observed that out of the DM patients seen with abnormal ACR, North-west and South-west zones have the least prevalence while South-east zone had the highest prevalence. The possible reason for the increased serum and urinary creatinine reported and the higher microalbuminuria (ACR) prevalence obtained could be linked to the irrigation and fishing culture adopted as a common business of the area. It is a well established fact that nephrotoxicity is the most common kidney problems and occurs when the body is exposed to the toxicants (Khan *et al*., 2013; Yassin and Al-shanti, 2016) in addition to the hyperglycaemic event in DM. With fishery activity as a well known business in Hadejia, people keeps flies away from the fresh fish displayed either for selling, drying or smoking. Some of the fishermen drives away flies using an insecticide named Dichlorvos (2,2-dichlorovinyl dimethyl phosphate) commonly known in local language as Pia-pia used for crop storage (Khan *et al*., 2013; Yassin and Al-shanti, 2016).

Considering gender differences among the patients in the present study, women had higher prevalence of microalbuminuria with significantly higher BMI compared to the men counterpart. This may suggest an increased risk of CKD among female when compared to the male patients. Similar report was presented by Collin *et al*. (1989), in a study involving 1184 diabetic and non-diabetic subjects that BMI has a significant relationship to albuminuria among residents of the Pacific Islands of Nauru with conclusion that urine ACR is strongly associated with insulin resistance and found stronger in women than men. Though inconsistent results were documented on the effect of gender on ACR in type 2 diabetic patients as reported by Raile *et al*. (2007), Hashim *et al*. (2004) have attributed the ACR complication to be pronounced among women as their result was consisted with the finding of this study. In a recent study in UK, a 1% difference in prevalence between men (6%) and women (7%) was demonstrated (Damsgard *et al*., 1990; Aitken *et al.,* 2014). Similarly, it has been indicated that elderly women have a worse outcome in the progression to end-stage renal disease and death compared to elderly men with type 2 DM (Ahmed and Ahmad, 2010).

It is believed that different carbohydrate-based foods have different effects on blood glucose and can be grouped based on the overall effect on the blood glucose levels as glycaemic index. Low glycaemic index foods such as lentils, beans and oats ought to supply glucose to the bloodstream in a stepwise pattern and leads to low stimulation of insulin release which may improve glycaemic control, compared to high glycaemic index foods (Thomas and Elliot, 2009) such as white bread, cassava, Maize, guinea-corn, yam or wheat flour. Management of DM is primarily aimed at improving blood glucose control that is associated with reduction in development and progression of complications and could possibly minimize medications, reduce risk of diabetic complications, improve quality of life and increase life expectancy.

Effective nutritional advice positively relates to blood glucose levels although presently there is no agreed optimal approach to the dietary treatment for DM. Controversy also marred the usefulness of glycaemic index (GI) in planning meal for diabetics. In a review by Thomas and Elliott

(2009), it was reported that glycaemic control in people with DM improve significantly with a low glycaemic index diet compared to those on higher glycaemic index diets or measured carbohydrate exchange diets.

Cocnlusion

In conclusion, although the reported prevalence was lower when compared with other values obtained in Nigerian, but yet alarming and enough to call the attention of policy makers and all other stakeholders in health to address and contribute in containing or minimizing the incidence of CKD. Gender, agricultural chemicals, poverty, DOD and possibly glycaemic status of our common staple foods play a vital role as risk factors in CKD progression. It is imperative to ascertain how agrochemicals are handled in those affected areas. This is the first study to come up with such relative conclusion despite the wide spread information in the community.

The study therefore recommend the policy makers to review how this agrochemicals are handled as well as providing means to reduce the impact of poverty by special intervention to those with the disease and mandate the health professional and researchers to assess the local foods for proper guide to the patients and their relatives.

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collection, management and analysis. All authors read and approved the final manuscript.

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