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SYSTEMATIC REVIEWS

Diabetic nephropathy in Africa: A systematic review

Jean Jacques N Noubiap, Jashira Naidoo, Andre P Kengne

Jean Jacques N Noubiap, Internal Medicine Unit, Edéa Regional Hospital, PO BOX 100 Edéa, Cameroon

Jashira Naidoo, Department of Medicine, Groote Schuur Hospital, University of Cape Town, 7925 Observatory, Cape Town, South Africa

Jashira Naidoo, Andre P Kengne, Non-Communicable Diseases Research Unit, South African Medical Research Council, 7505 Cape Town, South Africa

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Correspondence to: Andre P Kengne, Professor, Medical Research Council of South Africa, PO Box 19070 Tygerberg, 7505 Cape Town, South Africa. andre.kengne@mrc.ac.za Telephone: +27-21-9380529 Fax: +27-21-9380460

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Abstract

AIM: To determine the prevalence and incidence of diabetic nephropathy in Africa.

METHODS: We performed a systematic narrative review of published literature following the MOOSE Guidelines for Meta-Analysis and Systematic Reviews

of Observational Studies. We searched PubMed-MEDLINE for all articles published in English and French languages between January 1994 and July 2014 using a predefined strategy based on the combination of relevant terms and the names of each of the 54 African countries and African sub-regions to capture the largest number of studies, and hand-searched the reference lists of retrieved articles. Included studies reported on the prevalence, incidence or determinants of chronic kidney disease (CKD) in people with diabetes within African countries.

RESULTS: Overall, we included 32 studies from 16 countries; two being population-based studies and the remaining being clinic-based surveys. Most of the studies (90.6%) were conducted in urban settings. Methods for assessing and classifying CKD varied widely. Measurement of urine protein was the most common method of assessing kidney damage (62.5% of studies). The overall prevalence of CKD varied from 11% to 83.7%. Incident event rates were 94.9% for proteinuria at 10 years of follow-up, 34.7% for end-stage renal disease at 5 years of follow-up and 18.4% for mortality from nephropathy at 20 years of follow-up. Duration of diabetes, blood pressure, advancing age, obesity and glucose control were the common determinants of kidney disease.

CONCLUSION: The burden of CKD is important among people with diabetes in Africa. High quality data from large population-based studies with validated measures of kidney function are still needed to better capture the magnitude and characteristics of diabetic nephropathy in Africa.

Key words: Diabetes; Diabetes nephropathy; Chronic kidney disease; Epidemiology; Prevalence; Incidence; Mortality; Africa; Systematic review

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Core tip: Chronic kidney disease is a serious health threat for people with diabetes in Africa, with prevalence



figures ranging from 11% to 83.7%. The incidence estimates suggest that 95% of people with diabetes may have proteinuria after 10 years from diabetes diagnosis; about 35% may develop end-stage renal disease after 5 years and 18% die from nephropathy after 20 years of disease duration. Hypertension, obesity, poor glycemic control and diabetes duration are the main risk factors of chronic kidney disease among diabetic patients in Africa. High quality data are needed to refine the epidemiology of diabetic nephropathy on the continent.

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INTRODUCTION

Africa, like the rest of the world, is experiencing an increasing prevalence of diabetes alongside other non-communicable diseases, mainly as a result of urbanization, sedentary lifestyles, obesity and population growth and ageing^[1]. Estimates for 2013 by the International Diabetes Federation (IDF) indicate that the number of adults with diabetes in the world will expand by 55%, from 381.8 million in 2013 to 591.9 million in 2035^[2]. The largest increase of the population with diabetes will occur in sub-Saharan Africa, with a projected growth of 109.6%, from 19.8 million in 2013 to 41.5 million in 2035^[2].

Diabetes causes significant morbidity, disability and early mortality. Diabetes has been identified as a major contributor in several other important diseases, both non-communicable diseases such as cardiovascular disease and renal disease $^{\left[3,4\right] },$ and communicable diseases such as invasive bacterial infections^[5,6]. Mortality attributable to diabetes in sub-Saharan Africa was estimated to account for 8.6% of the total death in 2013^[7]. Diabetic nephropathy (DN) is one of the most common complications of diabetes. The prevalence of DN is increasing steeply along with the diabetes epidemic^[8]. Approximately one third to half of patients with diabetes develops renal manifestations^[8-11]. DN is associated with increased premature mortality, end-stage renal disease and need to renal replacement therapy, cardiovascular diseases, and escalating health-care costs^[8].

DN has been suggested to be more frequent among patients with diabetes in Africa as compared to those in the developed world due to delayed diagnosis, limited screening and diagnostic resources, poor control of blood sugar and other risk factors, and inadequate treatment at an early stage^[7,12,13]. However, evidence to support the burden of kidney diseases in people with diabetes in Africa remains very patchy, and we are not aware of any effort to synthesize existing data on the occurrence of kidney disease in African populations with diabetes. Accordingly, the aim of this review is to provide a comprehensive overview of the published evidence on the occurrence of nephropathy in African people with diabetes.

MATERIALS AND METHODS

Data sources and search strategy

A systematic narrative review of published literature was performed following the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies^[14]. We searched MEDLINE via PubMed for articles published in English and French on DN in Africa between January 1994 and July 2014, using a predefined strategy based on the combination of relevant terms and the names of each of the 54 African countries and African sub-regions to capture the largest number of studies. The data search was limited to human studies. The last search date was October 22, 2014. Search histories are provided in Table 1. Once duplicate references were removed the titles and abstracts of the references were screened. The references of included articles were scanned to identify additional articles of interest.

Study selection and data extraction

We included cross-sectional, case-control or cohort studies of subjects with diabetes mellitus resident in African countries reporting the prevalence or incidence or progression of DN. We excluded studies of populations of African origin residing outside Africa; case series (sample size less than 50 subjects), letters, comments and editorials; studies not published in English or French. Two investigators (JJNN, APK) independently identified articles and sequentially screened them for inclusion (Figure 1). Disagreements were solved by a third investigator (JN). Full text articles were reviewed by two investigators (JJNN and APK) who independently extracted data regarding study setting and design, study population characteristics and prevalence or incidence of DN.

RESULTS

We identified 730 articles, of which 73 were reviewed in full-text; 32 met the inclusion criteria (Figure 1)^[15-46].

Characteristics of included studies

Characteristics of the included studies are summarized in Table 2. The 32 studies were performed in 16 countries, with a geographical distribution covering all the African regions. However, more than half the studies [18 (56.3%)] were from South Africa (five), Nigeria (four), DR Congo (three) and Ethiopia (three).

Only two population-based studies were identified. In Democratic Republic of Congo, between March and April 2007, Makulo *et al*^[35] studied pathologic



Ta	ble 1 Search history PubMed	
Sea	arch Search terms	Hits
1	Diabetes[tw] OR Diabetes mellitus[tw] OR Type 1 diabetes[tw] OR Type 1 diabetes mellitus[tw] OR T1DM[tw] OR Type 2 diabetes[tw]] 445204
	OR Type 2 diabetes mellitus[tw] OR T2DM[tw] OR Hyperglycemia[tw] OR Glucose intolerance[tw]	
2	Renal insufficiency[tw] OR Renal failure[tw] OR Renal injury[tw] OR Renal disease[tw] Kidney insufficiency[tw] OR Kidney failure[tw] 154354
	OR Kidney injury[tw] OR Kidney disease[tw] OR End-stage renal disease[tw] OR End-stage renal failure[tw] OR End-stage kidne	y
	disease[tw] OR End-stage kidney failure [tw] OR End stage renal disease[tw] OR End stage renal failure[tw] OR End stage kidne	у
	disease[tw] OR End stage kidney failure [tw] OR Microalbuminuria [tw] OR Micro-albuminuria OR Macroalbuminuria [tw] or Macro	ı-
	albuminuria [tw]	
3	# 1 AND # 2	20388
4	Diabetic nephropathy [MeSH Terms]	19406
5	# 3 OR # 4	34221
6	((((("Africa"[MeSH] OR Africa*[tw] OR Algeria[tw] OR Angola[tw] OR Benin[tw] OR Botswana[tw] OR "Burkina Faso"[tw] O!	354928
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	Rwanda[tw] OR "Sao Tome"[tw] OR Senegal[tw] OR Seychelles[tw] OR "Sierra Leone"[tw] OR Somalia[tw] OR "South Africa"[tw] OR "S	it -
	Helena"[tw] OR Sudan[tw] OR Swaziland[tw] OR Tanzania[tw] OR Togo[tw] OR Tunisia[tw] OR Uganda[tw] OR "Western Sahara"[tw	1
	OR Zaire[tw] OR Zambia[tw] OR Zimbabwe[tw] OR "Central Africa"[tw] OR "Central African"[tw] OR "West Africa"[tw] OR "West	t
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	OR "Eastern African"[tw] OR "North Africa"[tw] OR "North African"[tw] OR "Northern Africa"[tw] OR "Northern African"[tw] OI	R
	"South African"[tw] OR "Southern Africa"[tw] OR "Southern African"[tw] OR "sub Saharan Africa"[tw] OR "sub Saharan African"[tw] OI	R
_	"subSaharan Africa"[tw] OR "subSaharan African"[tw]) NOT ("guinea pig"[tw] OR "guinea pigs"[tw] OR "aspergillus niger"[tw]))))	
7	# 5 AND # 6	1065
8	#4 Limits: 1994/01/01 to 2014/10/22 and studies done in Humans	918



Figure 1 Flow diagram of study selection.

albuminuria among 81 diabetic patients identified through a population-based survey on the prevalence of diabetes involving 1898 participants^[35]. Pruijm *et al*^[39] in Seychelles in 2004, conducted a largescale population-based estimate of the prevalence of microalbuminuria among 1218 adults. All other studies were clinic-based surveys conducted mostly in diabetic clinics. There were three cohort studies (two prospective and one retrospective), one case-control study and the other 28 studies were cross-sectional with non-random sampling. Only three (9.4%) studies were conducted in rural settings.

Methods of assessment and classification of chronic kidney disease (CKD) varied widely. The studies assessed kidney function by urine protein [20 (62.5%) studies], urine albumin-to-creatinine ration (ACR) [9 (28.1%) studies], and estimation of glomerular filtration rate (GFR) by Cockcroft-Gault formula [3 (9.4%) studies] or by MDRD formula [4 (12.4%) studies]. Six studies (18.8%) measured kidney function by two methods, and renal biopsy was not performed in any study.

Prevalence of CKD

As depicted in Table 3, the overall prevalence of CKD varied from 11% in Tunisia to 83.7% in Tanzania^[20,29]. In studies where proteinuria was used to assess CKD, the prevalence varied from 5.3% in South Africa to 53.1% in Cameroon (study with a small sample size)^[32,44]. When considering the estimation of the GFR, the prevalence ranged from 4.6% in Tanzania to 43.1% in Nigeria (study with a small sample size)^[15,33].

Incidence of CKD

A study in South Africa investigated the long-term incidence of proteinuria among T2DM patients. After 12 years of follow-up or death, 94.9% (56/59) had a proteinuria with a mean duration from diabetes onset to proteinuria of 9.7 (5.9) years^[31]. In another study in South Africa, found that 18.4% of T1DM patients had



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Ref.	Country	Period	Design	Setting 5	ample size	Mean or median age (yr)	Male	Type and duration of	Duration		Method for	CKD assessment	
							(%)	diabetes (yr)	5	Proteinuria	MDRD	Urine ACR Cock	croft-Gault
Motala <i>et al</i> ^[37] , 2001	South Africa	Not precised	Retrospective cohort study	Clinic, urban	219	39.5 T1DM; 58.4 T2DM	19.6	16.10 T1DM; 18.6 T2DM	At least 10 yr	persistent proteinuria (Dipstick)			
Elbagir <i>et al</i> ^[26] , 1995	Sudan	Jan-July 1992	Cross-sectional, self- selected sampling	Clinic, urban	128	31.5 (15-75)	48.4	Insulin-treated; 9 (1-40)	NA	Proteinuria (Dipstick)			
Sobngwi <i>et</i> al ^[14] , 1999	Cameroon	Not precised	Cross-sectional, self- selected sampling	Clinic, urban	64	37.4 normotensive T1DM; 51.7 normotensive T2DM; 57.9 hypertensive T1DM	57.8	6.7 normotensive T1DM; 4.7 normotensive T2DM;4.8 hypertensive T1DM	NA	Proteinuria			
Katchunga <i>et</i> al ^[30] , 2010	DR congo	2005-2007	Cross-sectional, self- selected sampling	Clinic, urban	98	58 (10.4)	35.7	7.3 T2DM	NA		MDRD (corrected for Blacks)		
Choukem <i>et</i> al ^[22] , 2012	Cameroon	Jan 2008- Oct 2010	Cross-sectional, self- selected sampling	Clinic, urban	420	56.7	49	4 (1-9) T2DM	NA	Proteinuria (Dipstick)			
Keeton <i>et al</i> ^[31] , 2004	South Africa	Not precised	Prospective cohort, self- selected sampling	Clinic, urban	59	62	35.6	17.8 T2DM	12 yr			Urine ACR	
Pruijm et al ^[39] , 2008	Seychelles	2004	Cross-sectional; random sex and age-stratified sample	Population 1	218 (whole sample, including diabetic patients)	Not precised	45.9	Newly diagnosed patients	ΝA			Urine ACR	
Alebiosu ^[16] , 2003	Nigeria	Jan 2000 June 2001	Cross-sectional, self- selected sampling	Clinic, urban	342	6.5 T1DM; 9.4 T2DM	53.8	26 T1DM; 53.4 T2DM	NA	Persistent proteinuria			
Bouaziz <i>et</i> al ^[20] , 2012	Tunisia	Jan 2008 Dec 2010	Cross-sectional, self- selected sampling	Clinic, urban	73	59.3	23.3	T2DM 10.6	NA	Proteinuria			
Ajayi <i>et al^[15]</i> , 2014	Nigeria	Not precised	Retrospective cross- sectional	Clinic, urban	65	Not available a	Not vailable	T2DM	NA		MDRD		
Levitt <i>et al</i> ^[32] , 1997	South Africa	July- December 1992	Cross-sectional, stratified random sampling	Clinic, urban	243	56.4	38.3	8 T2DM and T1DM	NA	Persistent proteinuria		Urine ACR	
Majaliwa <i>et</i> al ^[34] , 2007	Tanzania	June 2005- Feb 2006	Cross-sectional, self- selected sampling	Clinic, urban	66	12.6	42.4	4.76 T1DM	NA	Proteinuria			
Marshall <i>et</i> al ^[36] , 2013	Rwanda	June 2009-Nov 2010	Cross-sectional, self- selected sampling	Clinic, urban	286	18.6	46.5	3.4 TIDM	NA	Proteinuria		Urine ACR	
Alebiosu <i>et</i> al ^[18] , 2003	Nigeria	Sept 1999- August 2002	Cross-sectional, self- selected sampling	Clinic, urban	465	Not precised I	Not precised	T2DM	NA	Proteinuria			
Gill <i>et al</i> ^[28] , 2005	South Africa	From 1982 to 2002	Prospective cohort, self- selected sampling	Clinic, urban	88	22 at onset	52	TIDM	20 yr				
Djrolo <i>et al^[24]</i> , 2001	Benin	Not indicated	Cross-sectional	Clinic, urban	152	53.3	65.8	T1DM and T2DM	NA	Proteinuria			

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								Cockroft-Gault	Cockroft-Gault		Cockroft-Gault				
Urine ACR	Urine ACR				Urine ACR		Urine ACR						Urine ACR		
						MDRD							MDRD		
		Proteinuria	Albuminuria	Proteinuria		Proteinuria		Proteinuria		Proteinuria	Proteinuria	Proteinuria		Proteinuria	
NA	NA	NA	NA	NA	NA	5 yr	NA	NA	NA	NA	NA	NA	NA	NA	NA
42.2; T1DM and T2DM	57.6 T1DM	5.9 T1DM; 6.0 T2DM	10.3 T2DM	45 (range 30-69) T2DM and T1DM	T2DM and T1DM	17 (11-20) T1DM	7 T1DM and T2DM	11 T2DM	6 (3-11) T1DM (6.2%) and T2DM (93.8%)	T2DM	T1DM 3 (0-17) T2DM 4 (range 0-25)	11DM and 12DM; 53.4% less than 5 yr and 33.8% 5-9 yr	No precision	T1DM and T2DM 10.7	T2DM 9.4 cases, 5.5 controls
26.9	38.7	60	37	46.4	37.3	69.4	70.5	39.3	46.6	25	46.3	62.9	Not precised	28	50
56.5	19.1	31.4 T1DM; 56.7 T2DM	53.7	Not precised	50 (range 50-68)	29.5	41	60	54 (IQR 45-62)	54.7	T1DM 21(range 4-44.8) T2DM 53 (range 23.5-85)	44.4	Not precised	54.1	53.4
253	181	170	100	252	101	72	105	689	369	675	244	305	81	109	162
Clinic, rural	Clinic, urban	Clinic, urban	Clinic, urban	Clinic, urban/ urban (origin of participants)	Clinic, rural	Clinic, urban	Clinic, rural	Clinic, urban	Clinic, urban	Clinic, urban	Clinic, urban	Clinic, urban	Population- based, Urban	Clinic, urban	Clinic, urban
Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Prospective cohort study	Cross-sectional, self- selected sampling	Cross-sectional, self-	selected sampling Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Cross-sectional, self- selected sampling	Case (T2DM with persistent proteinuria- control (T2DM patients nephropathy)
1999	11 june 2008 to 30 july 2008	January - April 1995	June 2000 - January 2001	1 January 1993 - 10 August 1994	February - April 2011	From September 2006	Not precised	June 2006 -	July 2008 October 2011 - March 2012	August 2007 - June 2008	July 2003 - March 2004	October 2008	30 March - 24 April 2007	January - July 2005	January 2000 - June 2001
South Africa	DR congo	Ethiopia	Kenya	Uganda	Zambia	Morocco	Ethiopia	Tunisia	Tanzania	Ghana	Tanzania	Ethiopia	DR Congo	Ghana	Nigeria
Rotchford <i>et</i> al ^[43] , 2002	Rissassi <i>et al⁽⁴²⁾</i> , 2009	Rahlenbeck <i>et</i> al ^[40] , 1997	Wanjohi <i>et</i> al ^[45] , 2002	Nambuya <i>et</i> al ^[38] , 1996	Rasmussen <i>et</i> al ^[41] , 2013	Bentata <i>et al</i> ^[19] , 2013	Gill <i>et al</i> ^[27] , 2008	Bouzid et al ^[21] ,	2011 Janmohamed <i>et al^[29]</i> , 2013	Danquah <i>et</i> al ^[23] , 2012	Lutale <i>et al</i> ^[33] , 2007	Worku <i>et al</i> ^{ro} , 2010	Makulo <i>et al</i> ^[35] , 2010	Eghan <i>et al</i> ^[25] , 2007	Alebiosu <i>et</i> al ^{t17} , 2004

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ACR: Albumin-to-Creatinine Ratio; FUP: Follow-up; MDRD: Modification of diet renal disease; NA: Not applicable.

Table 3 Pre	valence an	d incid	ence of c	hronic kidn	ey disease in people with dia	abetes across studie	es in Africa	
Ref.	Country	Sample size	Type of diabetes	Duration of follow-up	Diagnostic criteria for CKD	Prevalence	Incidence	Comments
Motala <i>et</i> al ^[37] , 2001	South Africa	219	T1DM and T2DM	16.10 (4.9) T1DM; 18.6 (5.7) T2DM; at least 10	Persistent proteinuria (dipstix proteinuria on three or more consecutive occasions over 18 mo in the at absence of infection or cardiac failure)	Not applicable	24.6%	
Elbagir et al ^[26] , 1995	Sudan	128	Insulin- treated	Not applicable	Proteinuria (≥ 30 mg/dL)	22%	Not applicable	
Sobngwi <i>et</i> al ^[44] , 1999	Cameroon	64	T1DM and T2DM	Not applicable	Proteinuria	53.1%	Not applicable	
Katchunga et al ^[30] , 2010	DR Congo	98	T2DM	Not applicable	MDRD: CKD stage ≥ 2 according to the National Kidney foundation	18.1%	Not applicable	
Choukem <i>et</i> <i>al</i> ^[22] , 2012	Cameroon	420	T2DM	Not applicable	Proteinuria (30 mg/24 h)	31%	Not applicable	
Keeton <i>et</i> <i>al</i> ^[31] , 2004	South Africa	59	T2DM	12 yr	Urine Albumin-to-Creatinine Ratio (no detail)		After 12 yr of follow-up or death, 94.9% (56/59) had a proteinuria with a mean duration from diabetes onset to proteinuria of 9.7 (5.9) yr	83% (49/59) had an elevated SCr at the end of the study and in 66.1% (39/59) the SCr level had doubled during the study
Pruijm <i>et</i> <i>al</i> ^[39] , 2008	Seychelles	1218	All types	Not applicable	Microalbuminuria: Urine Albumin-to-Creatinine Ratio 3.4-33.9 mg albumin/mmol creatinine	36.1%	Not applicable	
Alebiosu ^[16] , 2003	Nigeria	342	T1DM and T2DM	Not applicable	Persistent proteinuria	28.4%	Not applicable	
Bouaziz et al ^[20] , 2012	Tunisia	73	T2DM	Not applicable	Microalbuminuria: < 2.8 g/mol for women and < 2.3 g/mol for men	11%	Not applicable	
Ajayi <i>et al</i> ^[15] , 2014	Nigeria	65	T2DM	Not applicable	MDRD: eGFR ≤ 60 mL/min per 1.73 m ²	43.1%	Not applicable	
Levitt <i>et al^[32],</i> 1997	South Africa	243	T2DM and	Not applicable	Urine Albumin-to-Creatinine Ratio > 3.4 mm/mmol	36.7%	Not applicable	
Majaliwa at	Tanzania	00	T1DM	Not	Persistent proteinuria (for at least 3 consecutive visits)	5.3%	Not applicable	
<i>al</i> ^[34] , 2007		99	TIDM	applicable		27.3 /0		
al ^[36] , 2013	Kwanua	200	TIDM	applicable	Albumin-to-Creatinine Ratio = 30-299 mg/g Macroalbuminuria or overt nephropathy: Urine Albumin- to-Creatinine Ratio ≥ 300 mg/g	Mcroalbuminuria: 21%; Macroalbuminuria: 5%	погаррисане	
Alebiosu <i>et</i> <i>al</i> ^[18] , 2003	Nigeria	465	T2DM	Not applicable	Proteinuria and eGFR	41.1%	Not applicable	The method for the estimation of the GFR is not indicated
Gill <i>et al</i> ^[28] , 2005	South Africa	88	T1DM	20 yr	Persistent dipstick proteinuria		Death of renal cause after 20 yr = 18.4% (9/49)	Death due to chronic renal failure after 20 yr of follow-up was 9/49 (after exclusion of lost to follow)
Djrolo <i>et al</i> ^[24] , 2001	Benin	152	T1DM and T2DM	Not applicable	Proteinuria (no detail)	20%	Not applicable	
Rotchford <i>et al</i> ^[43] , 2002	South Africa	253	T1DM and T2DM	Not applicable	Microalbuminuria > 2.5 mg/ mmol in men or 3.5 mg/mmol in women	46.4%	Not applicable	



Rissassi <i>et</i> <i>al</i> ^[42] , 2009	DR congo	181	T1DM	Not applicable	Microalbuminuria: Urine Albumin-to-Creatinine Ratio = 30-299 mg/g Macroalbuminuria: Urine Albumin-to-Creatinine Ratio ≥ 300 mg/g	21.9% (microalbuminuria) and 7.3% (macroalbuminuria)	Not applicable	
Rahlenbeck <i>et al</i> ^[40] , 1997	Ethiopia	170	T1DM and T2DM	Not applicable	Microalbuminuria: > 30 mg/L Macroalbuminuria: > 300 mg/L	T1DM: 32% (microalbuminuria) and 15% (macroalbuminuria) T2DM: 37% (microalbuminuria) and 20% (macroalbuminuria)	Not applicable	
Wanjohi et al ^[45] 2002	Kenya	100	T2DM	Not applicable	Proteinuria ≥ 20 mg	26%	Not applicable	
Nambuya <i>et</i> <i>al</i> ^[38] , 1996	Uganda	252	T1DM and T2DM	Not applicable	Proteinuria (no detail)	17.1%	Not applicable	Newly diagnosed patients
Rasmussen <i>et al</i> ^[41] , 2013	Zambia	101	T1DM and T2DM	Not applicable	Microalbuminuria: ACR = 3.5-35.0 for women and 2.5-25.0 mg/mmol for men Macroalbuminuria were ACR > 35.0 for women and > 25.0 for men	Microalbuminuria: 23.8% Macroalbuminuria: 8.9%	Not applicable	There were 33 patients with diabetes alone, and 68 patients with diabetes and hypertension
Bentata <i>et</i> <i>al</i> ^[19] , 2013	Morocco	72	T1DM	5 yr	Microalbuminuria: albumin excretion rate 30-300 mg/24 h Macroalbuminuria: albumin excretion rate > 300 mg/24 h Nephrotic proteinuria: albumin excretion rate ≥ 3000 mg/24 h Renal failure: eGFR < 60 mL/ min (MDRD)	At the time of enrollement Microalbuminuria: 48.6% Macroalbuminuria: 36.1% Nephrotic proteinuria: 15.3%	The incidence of end stage renal disease after 5 yr: 34.7%	Urinary assays done on admission were repeated on three specimens at three-monthly intervals
Gill <i>et al</i> ^[27] , 2008	Ethiopia	105	T1DM and T2DM	Not applicable	Nephropathy: ACR > 25.0 mg/mmol and retinopathy present Microalbuminuria: ACR > 2.5 and < 25.0 mg/mmol in men and > 3.5 and < 25.0 mg/mmol in women	Nephropathy: 2% Microalbuminuria: 51%		Urinary ACR levels (to assess microalbuminuria and nephropathy) were done on 59 patients, as those with haematuria and/or urinary infection were excluded
Bouzid <i>et</i> <i>al</i> ^[21] , 2011	Tunisia	689	T2DM	Not applicable	CKD: eGFR < 60 mL/min per 1.73 m ² (Cockroft-Gault) Microalbuminuria: albumin excretion rate 30-300 mg/24 h Macroalbuminuria: albumin excretion rate > 300 mg/24 h	CKD: 19.8% Microalbuminuria: 13% Macroalbuminuria: 10.1%	Not applicable	Macroalbuminuria was significantly associated with CKI (P < 0.00001)
Janmohamed et al ^[29] , 2013	Tanzania	369	T1DM and T2DM	Not applicable	CKD: eGFR < 60 mL/min per 1.73 m² (Cockroft-Gault) or microalbuminuria (> 20 mg/L) or overt protienuria	CKD: 83.7% eGFR < 60 mL/min per 1.73 m ² : 24.7% Microalbuminuria: 45.8% Overt proteinuria: 34.1%	Not applicable	
Danquah <i>et</i> al ^[23] , 2012	Ghana	671	T2DM	Not applicable	Proteinuria $\geq 20 \text{ mg/L}$	43%	Not applicable	
Lutale <i>et al</i> ^[33] , 2007	Tanzania	244	T1DM and T2DM	Not applicable	Microalbuminuria: AER 20-200 μg/min Macroalbuminuria: AER > 200 μg/min Renal failure: eGFR < 60 mL/ min per 1.73 m ² :	Microalbuminuria: 12.1% (T1DM); 9.8% (T2DM) Macroalbuminuria: 1.1% (T1DM); 7.2% (T2DM) Renal failure: 4.6% (T1DM); 22% (T2DM)	Not applicable	



	Worku <i>et</i> al ^[46] , 2010	Ethiopia	305	T1DM (38%) and T2DM (62%)	Not applicable	Proteinuria (no detail)	15.7%	Not applicable	
	Makulo et	DR Congo	81	No	Not	Microalbuminuria: ACR	Microalbuminuria:	Not applicable	
	al ^[35] , 2010			precision	applicable	30-299 mg/g	43.5%		
						Macroalbuminuria: ACR \geq	Macroalbuminuria:		
						300 mg/g	12%		
						Renal failure: $eGFR < 60 mL/$	Renal failure: 21.4%		
						min per 1.73 m ²			
	Eghan et al ^[25] ,	Ghana	109	T1DM	Not	Microalbuminuria: ACR	43.1%	Not applicable	
	2007			and	applicable	30-300 mg/g			
				T2DM					
	Alebiosu <i>et al</i> ^[17] , 2004	Nigeria	162	T2DM	Not applicable	Not applicable	Not applicable	Not applicable	The study did not assess the
									prevalence or
									incidence of diabetic
									nephropathy, but its
									predictors
-									

ACR: Albumin-to-Creatinine Ratio; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus; CKD: Chronic kidney disease; eGFR: Epidermal growth factor receptor.

died from renal nephropathy after 20 years of followup^[28]. In a recent study in Morocco, the incidence of end-stage renal disease after 5 years was $34.7\%^{[19]}$.

Risk factors of CKD

Twenty studies (62.5%) reported factors associated with CKD in diabetic patients (Table 4). However, in most studies the method to assess this association was imprecise. In cross-sectional studies, correlates of CKD included systolic and diastolic high blood pressure, long duration of diabetes, older age, dyslipidemia, obesity^[16-22,25,26,29-31,33,36,40,42-44,46]. In a study in Cameroon, T2DM patients with systolic hypertension and diastolic hypertension were respectively 1.45 (95%CI: 1.15-1.84; P = 0.006) and 1.33 (95%CI: 1.06-1.66; P = 0.026) times more likely to have nephropathy^[22]. Two studies in Rwanda and South Africa respectively showed that a one year increase in the duration of T1DM increased by 0.86 (95%CI: 0.77-0.96; P =0.008) the odds of microalbuminuria $^{\scriptscriptstyle [36]}$, and that T1DM and T2DM patients with a duration of diabetes greater than 10 years were 4.19 times (95%CI: 1.93-9.10; P < 0.001) more likely to have microalbuminuria^[43]. Poor glycemic control as measured by HbA1c was also a strong predictor of nephropathy. For instance, HbA1c level greater than 10% and 14% were respectively associated with a 2.6 fold (95%CI: 1.1-6.4) and a 4.69 (95%CI: 1.65-13.3; P = 0.004)^[42,43]. A 1 g/dL decrease in hemoglobin level has been found to be associated with end-stage renal disease (OR 3.18, 95%CI: 1.47-6.87; P = 0.003)^[19]. Studies in Nigeria showed that left ventricular hypertrophy, stroke, myocardial infarction and peripheral arterial disease were more frequent in T2DM patients with nephropathy, especially those with advanced stages^[17,18].

DISCUSSION

Diabetic nephropathy is a common and morbid com-

plication of diabetes and the leading cause of CKD in the developed world. The lack of renal registries means that there are no reliable statistics about the burden of CKD in people with diabetes in the majority of African countries. The current systematic review identified 32 relevant studies published over the last 20 years on kidney diseases in people with diabetes residing in Africa. Prevalence rates ranged from 11% to 83.7% for the overall CKD, 5.3% to 53.1% for CKD based on proteinuria, and 4.6% to 43.1% for CKD based on eGFR. Incident event rates were 94.9% for proteinuria at 10 years for follow-up, 34.7% for ERSD at 5 years of follow-up and 18.4% for mortality from nephropathy at 20 years of followup. Diagnosed duration of diabetes, blood pressure variables, advancing age, obesity and to some extend glucose control were the common determinants of kidney disease in people with diabetes. Studies were overwhelmingly hospital-based studies; half of them originated from four countries while variable definitions and methods for assessing nephropathy had been used across studies.

The most recent overview of CKD in populations within Africa was completed in 2012, and was restricted to sub-Saharan African Countries^[47]. This review identified 90 articles representing data from 21 countries, with over half of the studies originating from South Africa, Nigeria and Ethiopia alones. Across 21 studies deemed to be of medium to high quality by the investigators, the pooled prevalence of CKD was 13.9% (95%CI: 12.2-15.7), with substantial heterogeneity across studies. The prevalence in people with diabetes ranged from 4% to 24% based essentially on proteinuria defined CKD^[47]. In our review without applying quality criteria, we found much higher prevalence of CKD, regardless of the definition. In four studies published in 2013 for instance, the prevalence of microalbuminuria ranged between 21% and 45%. Although issues with the quality of the studies preclude direct comparisons, it is likely that nephropathy is

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Table 4 Ris	k factors fo	r chronic kid	dney disease in pe	ople with diabetes					
Ref.	Country	Sample size	Type of diabetes	Diagnostic criteria for CKD	Risk factor	Measure of assoc	iation	Factors adjusted for	Comments
						Effect size	<i>P</i> -value		
Motala <i>et al</i> ^[37] , 2001	South Africa	219	T1DM and T2DM	Persistent proteinuria	Not assessed				
Elbagir <i>et</i>	Sudan	128	Insulin-treated	Proteinuria	Age		P = 0.006		
al ¹²⁰ , 1995					Duration of diabetes Svstolic BP		P = 0.003 P = 0.0001		
					Diastolic BP		P = 0.001		
Sobnowi et	Cameroon	64	T1DM and T2DM	Proteinuria	Serum cholesterol Duration of diabetes		P < 0.05 P = 0.04		
al ^[44] , 1999					Diastolic BP		P = 0.01		
Katchunga <i>et</i> al ^[30] , 2010	DR Congo	8	T2DM	MDRD (corrected for Blacks); CKD stage ≥ 1 according to the National Kidney foundation	Hypertension	aOR: 2.49 (0.98-6.34)	P = 0.04	Age, duration of diabetes, BMI	
Choukem et	Cameroon	420	T2DM	Proteinuria $(30 \text{ mg}/24 \text{ h})$	Systolic BP	aOR: 1.45 (1.15-1.84)	P = 0.006		
at', 2012					Diastolic bl' Pulse pressure	aOR: 1.35 (1.06-1.66) aOR: 1.35 (1.06-1.71)	P = 0.0007 P = 0.0007		
					Mean arterial pressure	aOR: 1.42 (1.13-1.78)	P = 0.006		
Keeton <i>et</i>	South	59	T2DM	Urine Albumin-to-Creatinine Ratio	High entry serum creatinine		P < 0.006		These are risk factors for death from
al ^[31] , 2004	Africa			(no detail)	BMI < 28		P < 0.003		chronic renal failure (compared with the
					Severe retinopathy		P < 0.002		patients who were still alive at follow-up)
					Mean glucose level of > 14		P < 0.035		
					mmol/L				By the end of study 47 of the 59 patients
									had died; the cause of death not
									established in 2 patients. Death was due to
Pruiim of al ^[39]	Savchallas	1718	All tymes	Microalbuminuria: Hrine Albumin-	Not acceced				CITOTIC FERTIALITY IN 17 CASES Risk factors were investigated in the
2008			and former	to-Creatinine Ratio 3.4-33.9 mg					whole study population in both diabetics
2				albumin/mmol creatinine					and non-diabetics
Alebiosu ^{l16]} , 2003	Nigeria	342	T1DM and T2DM	Persistent proteinuria	Not assessed				
Bouaziz et	Tunisia	73	T2DM	Microalbuminuria: < 2.8 g/mol for	Family history of		P = 0.0289		Comparison of T2DM patients with
al ^[20] , 2012				women and $< 2.3 \text{ g/mol for men}$	nephropathy				nephropathy with those without
					Smoking		P = 0.0056		nephropathy
					Insulin therapy		P = 0.0310		
					Glitazones therapy		P = 0.0115		
					Anti-hypertensives (not ACE inhibitor)		<i>P</i> < 0.0001		
					Lipid-lowering agents		P < 0.0001		
Ajayi <i>et al</i> ^[15] , 2014	Nigeria	65	T2DM	MDRD: eGFR ≤ 60 mL/ min per 1.73 m ²	Not assessed				
Levitt et al ^[32] .	South	243	T2DM and T1DM	Urine Albumin-to-Creatinine Ratio	Not assessed				
1997	Africa	1		> 3.4 mm/mmol					
				and Persistent proteinuria (for at					
				least 3 consecutive visits)					

Majaliwa <i>et</i> _{al^[34] 2007}	Tanzania	66	TIDM	Proteinuria (no detail)	Missing insulin doses		P = 0.045	Not available	
Marshall et $al^{[36]}$, 2013	Rwanda	286	TIDM	Microalbuminuria: Urine Albumin- to-Creatinine Ratio = 30-299 mg/ g	Age (increase)	aOR: 0.86, 95% CI: 0.77-0.96	<i>P</i> = 0.009	Each variable is adjusted for the others	These are risk factors of microalbuminuria. There was no factor
					Duration of diabetes (one year increase)	aOR: 0.86, 95% CI: 0.77-0.96	P = 0.008		associated to macroalbuminuria
					Diastolic Dr (increase)	aux: 0.00, 93%u: 0.77-0.96	F = 0.004		
					HBA1c (increase)	aOR: 0.86, 95% CI: 0.77-0.96	P = 0.047		
Alebiosu <i>et</i> al ⁽¹⁸⁾ , 2003	Nigeria	465	T2DM	Proteinuria and eGFR (no detail)	Hypertension, left ventricular hypertrophy, stroke and myocardial infarction were more frequent in advanced stages	Not available	<i>P</i> < 0.05	Not available	Patients with advanced stages of nephropathy (IV and V) were compared with those with stages ≤ III
Gill <i>et al</i> ^[28] , 2005	South Africa	88	TIDM	Persistent dipstick proteinuria	Not assessed				
Djrolo et al ^[24] , 2001	Benin	152	T1DM and T2DM	Proteinuria (no detail)		Not available	Not available	Not available	Proteinuria was more frequent in insulin- treated patients compared those on oral antidiabetic treatment. The prevalence of proteinuria also increased with the duration of diabetes
Rotchford <i>et</i> al ^[43] , 2002	South Africa	253	T1DM and T2DM	Microalbuminuria > 2.5 mg/mmol in men or 3.5 mg/mmol in women	Duration of diabetes > 10 yr BMI > 33 HbA1c > 14% Hynertension	4.19 (1.93-9.10) 0.27 (0.08-0.48) 4.69 (1.65-13.3) 2.11 (1.07-4.17)	< 0.001 0.002 0.004 0.031	Model contains duration of diabetes, BMI, HbA1c, age and hymertension	
Rissassi <i>et</i> al ^[42] , 2009	DR congo	181	TIDM	Microalbuminuria: Urine Albumin- to-Creatinine Ratio = 30-299 mg/g Macroalbuminuria: Urine Albumin- to-Creatinine Ratio ≥ 300 mg/g	Duration of diabetes > 5 yr Age > 18 yr HbA1c > 10%	2.6 (1.1-6.4) 2.6 (1.1-6.4)		No precision	
Rahlenbeck <i>et</i> al ^[40] , 1997	Ethiopia	170	T1DM and T2DM	albuminuria: > 30 mg/L	Duration of diabetes Systolic blood pressure	Beta = 0.061, SE = 0.018 for T1DM Beta = 0.027, SE = 0.005 for T1DM	< 0.001 < 0.001 <	Hypertensive patients excluded	
Wanjohi <i>et</i> al ^[45] , 2002	Kenya	100	T2DM	Proteinuria ≥ 20mg	None identified				
Nambuya <i>et</i> al ^[38] , 1996	Uganda	252	T1DM and T2DM	Proteinuria (no detail)	None assessed				
Rasmussen <i>et</i> al ^[41] ,2013	Zambia	101	T1DM and T2DM	Microalbuminuria: ACR = 3.5-35.0 for women and 2.5-25.0 mg/mmol for men Macroalbuminuria were ACR	None assessed				
Bentata <i>et</i> al ^[19] , 2013	Maroc	72	MULT	End-stage renal disease: eGFR < 15 mL/min	Hemoglobin blood (per 1 g/dL decrease) Diastolic blood pressure (per 1 mmHg increase)	3.18 (1.47-6.87) 1.15 (1.04-1.27)	0.003	No precision	These are independent risk factors for ESRD in type-1 diabetes patients with diabetic nephropathy

		Measure of association is β			The associations were assessed by comparing patients with and without microalbuminuria	The study assessed the predictors of diabetic nephropathy comparing T2DM patients with and without nephropathy
	Adjustment made, but no precision	Predictors in the	model: diabetes duration, Systolic BP, age, serum creatinine			
 < 0.00001 < 0.00001 < 0.0001 < 0.001 < 0.001 0.01 	0.03	< 0.0001	0.010 0.016 0.001 0.018		0.04 0.05 0.01 0.0061	 < 0.05 < 0.05 < 0.05 < 0.05
Not provided	1.03 (1.00-1.05)	0.090 (0.049- 0.131)	0.012 (0.003-0.021) 0.011 (0.002- 0.020) Not provided			
None assessed Older age Hypertension Long duration of diabetes Higher BMI Dvslividemia	Older age	Duration of diabetes	Elevated systolic blood pressure Elevated serum creatinine Duration of diabetes T2DM on insulin	Not assessed	Duration of diabetes Serum creatinine Blood urea nitrogen Urine potassium	Duration of diabetes Serum total cholesterol Alcohol > 30 mg/ d Peripheral vascular disease Stroke
Nephropathy: ACR > 25.0 mg/mmol and retinopathy Microalbuminuria: ACR > 2.5 and < 25.0 mg/mmol in men and > 3.5 and < 25.0 mg/mmol in women < 25.0 mg/mmol in women Renal failure: creatinine clearance < 60 mL/min (Cockroft-Gault)	CKD: eGFR < 60 mL/min per 1.73 m ² (Cockroft-Gault) or microalbuminuria (> 20 mg/L) or overt proteinuria	Abnormal proteinuria: AER > 20	µg/min Proteinuria (no detail)	viicroalpuminuria: ACK 30-299 mg/ g Macroalbuminuria: ACR ≥ 300 mg/g Renal failure: 6GFR < 60 mL/min per 1.73 m ²	Microalbuminuria: ACR 30-300 mg/ g	No precision
T1DM and T2DM T2DM	T1DM and T2DM	T1DM and T2DM	T1DM and T2DM	No precision	TIDM and T2DM	T2DM
105 689	369	244	305	70	109	162
Ethiopia Tunisia	Tanzania	Tanzania	Ethiopia	DK Congo	Ghana	Nigeria
Gill <i>et a</i> $^{l^{22}}$, 2008 Bouzid <i>et</i> $al^{[21]}$, 2011	Janmohamed et al ^[29] , 2013 Danmah et	$al^{[23]}$, 2012 Lutale <i>et al</i> ^[33] ,	2007 Worku <i>et al⁽⁴⁶⁾</i> , 2010	makuto <i>et</i> al ¹⁵³ , 2010	Eghan <i>et al^{l25]},</i> 2007	Alebiosu <i>et</i> al ¹¹⁷ , 2004

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more frequent in population with diabetes within Africa than in developed countries. The review by Stanifer *et* $al^{[47]}$ also identified many challenges and limitations, which largely apply to the current study.

The most important aspect in assessing incidence and prevalence of diabetic nephropathy in Africa is currently different diagnostic criteria for CKD. There are no clear definitions on DN. The 2012 KDIGO CKD classification assesses diabetes related kidney changes according to urinary albumin-to-creatinine ratio based on early morning spot urine samples^[48]. Quantification of proteinuria in assessing CKD is controversial as no optimal test exists. The National Institute for Health and Clinical Excellence (NICE) guidance has recommended that an early morning urinary ACR should be preferred to other tests of proteinuria, because ACR offers greater sensitivity for the detecting lower, but clinically significant, levels of proteinuria^[49]. Almost all the studies included in our review utilized urine tests to diagnose CKD, but only nine studies used ACR. Inconsistencies in the way and manner of reaching a diagnosis of DN in Africans are explained at least in part by issues relating to availability and accessibility of screening or diagnostic tools. Swanepoel et al^[50] have reviewed in detail some of the problems associated with nephrology in Africa and discussed the role of lack of amenities in diagnosing renal diseases. Another challenge to making the diagnosis of diabetic nephropathy in Africa is the degree to which other causes of chronic kidney disease have been excluded. A standard armamentarium of tests would include tests looking for HIV, hepatitis B and C, brief collagen screen, syphilis exclusion and other tests would have to be based on history and physical exam.

The classification of CKD is important in the definition of DN and has a few limitations that are universally acknowledged: eGFR underestimates kidney function and there is discordance in the estimates across different estimators^[51]; isolated microalbuminuria is a normal feature of aging, inflammation, vascular pathologies, smoking, diet and obesity which are all frequent in diabetes; decline in kidney function is an expected phenomenon with advanced age, just like diabetes risk increases with age. Further considerations to CKD classifications and DN definition limitations is that current guidelines take no notice of the single most important risk factor associated with CKD namely hypertension, which is present in over 50% of people with type 2 diabetes.

Risk factor association was not assessed in 12 of the 32 studies, however common risk factors included were hypertension, raised BMI, HbA1c and duration of diabetes. Despite advances in management over the last three decades, many people with diabetes still develop CKD. This may be partly explained by the poor achievement of blood pressure and blood glucose targets. Recently the JNC 8 guidelines have added to the controversy of various blood pressure targets needed for diabetic patients that would assist in preventing progression to CKD. Optimal targets when reached, however have shown to aid in progression to progression. Another risk factor pertinent to the developing world is the socioeconomic status of individuals in the causative role of diabetic nephropathy. Weil *et al*⁽⁵²⁾, in 2010 reviewed factors associated with disadvantage that may increase the risk of diabetic kidney disease, and the barriers to care that hinder attempts to provide an adequate therapeutic response^[52].

Several mechanisms underlying the pathogenesis of diabetic nephropathy have been suggested and include glomerular hyperfiltration; hyperglycemia and the increased production of advanced glycation end products; hypoxia-inflammation and the activation of cytokines. Hyperfiltration commonly occur in early in the course of diabetes and involves glucose-dependent dilation of the afferent arteriolar dilation, and the enhanced filtration area secondary to the increase in the number of mesangial cells and capillary loops. Molecular level action involves vasoactive mediators like insulin-like growth factor 1, transforming growth factor beta, nitric oxide, prostaglandin, glucagon and vascular endothelial growth factor^[53]. Other hallmarks of diabetic nephropathy include nodular diabetic glomerulosclerosis and diffuse glomerulosclerosis, mediated at least in part by inflammatory processes and immune cells activity^[53]. Interstitial fibrosis and tubular atrophy are also seen early in DN, with the underlying pathogenetic mechanism being similar to those in progressive non diabetic renal disease^[54].

Diabetic nephropathy ultimately occurs only in susceptible individuals with diabetes; which susceptibility is determined by the combined effect of genetic predisposition and non-genetic factors. Genetic susceptibility to diabetic nephropathy is by nature polygenetic. Whole-genome scanning studies have identified several chromosomal regions linked with diabetic nephropathy; however, the pathophysiologic function of such genetic regions has yet to be fully elucidated. Genetic polymorphisms may explain the familial clustering of diabetic nephropathy^[55]. Some studies have suggested some detrimental effect of the double-deletion (DD) polymorphism of the angiotensinconverting enzyme (ACE) genotype on disease progression^[56]. Non-genetic determinants of diabetic nephropathy include among others socioeconomic factors, dietary factors, poor hyperglycemic control, hypertension, obesity and early life factors^[57,58]. Hypertension appears to be a strong correlate of disease progression in Black people^[59,60].

The current review has some limitations. Included studies were mostly based on small samples, with different study designs and most of the studies were cross sectional with only two being retrospective cohorts and one case-control. A large proportion were based in urban clinics with and most of the populations studied were that attending a general diabetic clinic and the results may not be generalizable

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to primary care populations. Ideally chronic kidney disease should not be diagnosed on the basis of single measurements of serum creatinine and albuminuria, and standard baseline investigations are needed to exclude other causative kidney disease, although there is precedence for this in other studies in the West as well. Finally, detection of microalbuminuria was one the most frequent method to assess the presence of diabetic nephropathy. As microalbuminuria is more a quantitative estimate of endothelial/vascular dysfunction than of diabetic nephropathy, the incidence and prevalence rate of diabetic nephropathy have probably been overestimated when assessing kidney function by urine protein.

In conclusion, the current review gives a small glimpse of the larger numbers of CKD in diabetics in Africa compared to Western society. CKD is a substantial health burden among diabetic patients on the African continent, with prevalence varying from 11% to 83.7% depending on the method of assessment. Estimates suggest that 95% of diabetics may have proteinuria after a 10 years duration of diabetes, about 35% may have an end-stage renal disease after 5 years and 18% die from nephropathy after 20 years of disease duration. Risk factors of CKD include mainly hypertension, obesity, poor glycemic control and disease duration. Better surveillance of diabetes is a necessary first step toward its prevention and control, which is now recognized as an urgent priority. An electronic database in African regions would be ideal to assist in this entity although it is presumed that we are light years away from that. At a primary care level it is very plausible that with early detection, proper screening, and management, the impact of diabetic nephropathy may be better mitigated to lessen its impact on society and healthcare.

COMMENTS

Background

African countries are experiencing an epidemics of diabetes mellitus. Diabetic nephropathy is one the most frequent complications of diabetes mellitus. Several studies on the epidemiology of diabetic nephropathy have been conducted in Africa, but there is no previous published work which synthesizes evidences from this study to provide an overview of the disease on the continent.

Research frontiers

Epidemiological data on diabetic nephropathy in Africa are sparse. These data are important to quantify the magnitude of the disease and assist the formulation of strategies to reduce the impact of nephropathy on people with diabetes in Africa.

Innovations and breakthroughs

This review is the first to synthesize relevant data on diabetic nephropathy in Africa. The authors performed extensive electronic and manual bibliographic searches to determine the prevalence and incidence of diabetic nephropathy on the continent. Although the quality of data was not optimal, estimates suggest that the prevalence of diabetic nephropathy vary between 11%-83.7%. About one third of diabetic patients have end-stage renal disease after 5 years and about one fifth die from nephropathy after 20 years of disease duration. Hypertension, obesity, poor glycemic control and disease duration are the main risk factors of chronic kidney disease among diabetic patients in Africa.

Applications

This review shows that the burden of chronic kidney disease is important among people with diabetes in Africa. The findings will have implications for policy, practice and future research on diabetic nephropathy on the continent.

Terminology

Diabetic nephropathy is an alteration of the function of the kidneys due to diabetes mellitus. It is associated with substantial morbidity and mortality.

Peer-review

The authors of the present manuscript performed extensive electronic and manual bibliographic research to determine the prevalence and incidence of kidney disease in people with diabetes mellitus within countries in Africa. Overall the review is well written.

REFERENCES

- Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001; 414: 782-787 [PMID: 11742409 DOI: 10.1038/414782a]
- 2 Aguiree F, Brown A, Cho NH, Dahlquist G, Dodd S, Dunning T, Hirst M, Hwang C, Magliano D, Patterson C, Scott C, Shaw J, Soltesz G, Usher-Smith J, Whiting D. IDF Diabetes Atlas: sixth edition. 6th ed. Basel, Switzerland: International Diabetes Federation, 2013
- 3 Seshasai SR, Kaptoge S, Thompson A, Di Angelantonio E, Gao P, Sarwar N, Whincup PH, Mukamal KJ, Gillum RF, Holme I, Njølstad I, Fletcher A, Nilsson P, Lewington S, Collins R, Gudnason V, Thompson SG, Sattar N, Selvin E, Hu FB, Danesh J. Diabetes mellitus, fasting glucose, and risk of cause-specific death. *N Engl J Med* 2011; 364: 829-841 [PMID: 21366474 DOI: 10.1056/NEJMoa1008862]
- 4 Fox CS, Matsushita K, Woodward M, Bilo HJ, Chalmers J, Heerspink HJ, Lee BJ, Perkins RM, Rossing P, Sairenchi T, Tonelli M, Vassalotti JA, Yamagishi K, Coresh J, de Jong PE, Wen CP, Nelson RG. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. *Lancet* 2012; **380**: 1662-1673 [PMID: 23013602 DOI: 10.1016/S0140-6736(12)61350-6]
- 5 Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. *PLoS Med* 2008; 5: e152 [PMID: 18630984 DOI: 10.1371/journal. pmed.0050152]
- 6 Muller LM, Gorter KJ, Hak E, Goudzwaard WL, Schellevis FG, Hoepelman AI, Rutten GE. Increased risk of common infections in patients with type 1 and type 2 diabetes mellitus. *Clin Infect Dis* 2005; 41: 281-288 [PMID: 16007521 DOI: 10.1086/431587]
- 7 Kengne AP, Echouffo-Tcheugui JB, Sobngwi E, Mbanya JC. New insights on diabetes mellitus and obesity in Africa-part 1: prevalence, pathogenesis and comorbidities. *Heart* 2013; 99: 979-983 [PMID: 23680891 DOI: 10.1136/heartjnl-2012-303316]
- Harjutsalo V, Groop PH. Epidemiology and risk factors for diabetic kidney disease. *Adv Chronic Kidney Dis* 2014; 21: 260-266 [PMID: 24780453 DOI: 10.1053/j.ackd.2014.03.009]
- 9 Assogba GF, Couchoud C, Roudier C, Pornet C, Fosse S, Romon I, Druet C, Stengel B, Fagot-Campagna A. Prevalence, screening and treatment of chronic kidney disease in people with type 2 diabetes in France: the ENTRED surveys (2001 and 2007). *Diabetes Metab* 2012; **38**: 558-566 [PMID: 23036461 DOI: 10.1016/ j.diabet.2012.08.004]
- 10 Bakris GL. Recognition, pathogenesis, and treatment of different stages of nephropathy in patients with type 2 diabetes mellitus. *Mayo Clin Proc* 2011; 86: 444-456 [PMID: 21531886 DOI: 10.4065/mcp.2010.0713]
- 11 Thomas MC, Weekes AJ, Broadley OJ, Cooper ME, Mathew TH. The burden of chronic kidney disease in Australian patients with type 2 diabetes (the NEFRON study). *Med J Aust* 2006; 185: 140-144 [PMID: 16893353]
- 12 **Kengne AP**, Sobngwi E, Echouffo-Tcheugui JB, Mbanya JC. New insights on diabetes mellitus and obesity in Africa-Part 2:

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prevention, screening and economic burden. *Heart* 2013; **99**: 1072-1077 [PMID: 23680890 DOI: 10.1136/heartjnl-2013-303773]

- 13 Mbanya JC, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in sub-Saharan Africa. *Lancet* 2010; **375**: 2254-2266 [PMID: 20609971 DOI: 10.1016/S0140-6736(10)60550-8]
- 14 Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Metaanalysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-2012 [PMID: 10789670]
- 15 Ajayi S, Mamven M, Ojji D. eGFR and chronic kidney disease stages among newly diagnosed asymptomatic hypertensives and diabetics seen in a tertiary health center in Nigeria. *Ethn Dis* 2014; 24: 220-225 [PMID: 24804370]
- 16 Alebiosu CO. Clinical diabetic nephropathy in a tropical African population. *West Afr J Med* 2003; 22: 152-155 [PMID: 14529227]
- 17 Alebiosu CO, Odusan O, Familoni OB, Jaiyesimi AE. Cardiovascular risk factors in type 2 diabetic Nigerians with clinical diabetic nephropathy. *Cardiovasc J S Afr* 2004; 15: 124-128 [PMID: 15258622]
- 18 Alebiosu CO, Odusan O, Jaiyesimi A. Morbidity in relation to stage of diabetic nephropathy in type-2 diabetic patients. *J Natl Med Assoc* 2003; 95: 1042-1047 [PMID: 14651370]
- 19 Bentata Y, Haddiya I, Latrech H, Serraj K, Abouqal R. Progression of diabetic nephropathy, risk of end-stage renal disease and mortality in patients with type-1 diabetes. *Saudi J Kidney Dis Transpl* 2013; 24: 392-402 [PMID: 23538374]
- 20 Bouaziz A, Zidi I, Zidi N, Mnif W, Zinelabidine HT. Nephropathy following type 2 diabetes mellitus in Tunisian population. West Indian Med J 2012; 61: 881-889 [PMID: 24020228]
- 21 Bouzid C, Smida H, Kacem A, Turki Z, Ben Salem L, Ben Rayana C, Slama BC. [Renal failure in Tunisian patients with type 2 diabetes: frequency and related factors]. *Tunis Med* 2011; 89: 10-15 [PMID: 21267820]
- 22 Choukem SP, Dzudie A, Dehayem M, Halle MP, Doualla MS, Luma H, Kengne AP. Comparison of different blood pressure indices for the prediction of prevalent diabetic nephropathy in a sub-Saharan African population with type 2 diabetes. *Pan Afr Med* J 2012; **11**: 67 [PMID: 22655101]
- 23 Danquah I, Bedu-Addo G, Terpe KJ, Micah F, Amoako YA, Awuku YA, Dietz E, van der Giet M, Spranger J, Mockenhaupt FP. Diabetes mellitus type 2 in urban Ghana: characteristics and associated factors. *BMC Public Health* 2012; **12**: 210 [PMID: 22429713 DOI: 10.1186/1471-2458-12-210]
- 24 Djrolo F, Attolou VG, Avode DG, Houngbe F, Akpona S, Addra B, Kodjoh N. [Diabetic nephropathy: an epidemiological study based on proteinuria in a population of black African diabetics in Cotonou, Benin]. *Sante* 2001; 11: 105-109 [PMID: 11440886]
- 25 Eghan BA, Frempong MT, Adjei-Poku M. Prevalence and predictors of microalbuminuria in patients with diabetes mellitus: a cross-sectional observational study in Kumasi, Ghana. *Ethn Dis* 2007; 17: 726-730 [PMID: 18072386]
- 26 Elbagir MN, Eltom MA, Mahadi EO, Berne C. Pattern of longterm complications in Sudanese insulin-treated diabetic patients. *Diabetes Res Clin Pract* 1995; 30: 59-67 [PMID: 8745207]
- 27 Gill G, Gebrekidan A, English P, Wile D, Tesfaye S. Diabetic complications and glycaemic control in remote North Africa. *QJM* 2008; 101: 793-798 [PMID: 18687702 DOI: 10.1093/qjmed/ hcn096]
- 28 Gill GV, Huddle KR, Monkoe G. Long-term (20 years) outcome and mortality of Type 1 diabetic patients in Soweto, South Africa. *Diabet Med* 2005; 22: 1642-1646 [PMID: 16401306 DOI: 10.1111/ j.1464-5491.2005.01712.x]
- 29 Janmohamed MN, Kalluvya SE, Mueller A, Kabangila R, Smart LR, Downs JA, Peck RN. Prevalence of chronic kidney disease in diabetic adult out-patients in Tanzania. *BMC Nephrol* 2013; 14: 183 [PMID: 24228774 DOI: 10.1186/1471-2369-14-183]
- 30 Katchunga P, Hermans MP, Manwa B, Lepira F, Kashongwe Z, M'Buyamba-Kabangu JR. [Hypertension, insulin resistance and chronic kidney disease in type 2 diabetes patients from South Kivu,

DR Congo]. Nephrol Ther 2010; 6: 520-525 [PMID: 20605543 DOI: 10.1016/j.nephro.2010.04.002]

- 31 Keeton GR, Smit Rv, Bryer A. Renal outcome of type 2 diabetes in South Africa--a 12-year follow-up study. S Afr Med J 2004; 94: 771-775 [PMID: 15487844]
- 32 Levitt NS, Bradshaw D, Zwarenstein MF, Bawa AA, Maphumolo S. Audit of public sector primary diabetes care in Cape Town, South Africa: high prevalence of complications, uncontrolled hyperglycaemia, and hypertension. *Diabet Med* 1997; 14: 1073-1077 [PMID: 9455936 DOI: 10.1002/(sici)1096-9136(1997 12)14]
- 33 Lutale JJ, Thordarson H, Abbas ZG, Vetvik K. Microalbuminuria among Type 1 and Type 2 diabetic patients of African origin in Dar Es Salaam, Tanzania. *BMC Nephrol* 2007; 8: 2 [PMID: 17224056 DOI: 10.1186/1471-2369-8-2]
- 34 Majaliwa ES, Munubhi E, Ramaiya K, Mpembeni R, Sanyiwa A, Mohn A, Chiarelli F. Survey on acute and chronic complications in children and adolescents with type 1 diabetes at Muhimbili National Hospital in Dar es Salaam, Tanzania. *Diabetes Care* 2007; 30: 2187-2192 [PMID: 17563337 DOI: 10.2337/dc07-0594]
- 35 Makulo R, Nseka MN, Jadoul M, Mvitu M, Muyer MT, Kimenyembo W, Mandja M, Bieleli E, Mapatano MA, Epira FB, Sumaili EK, Kaimbo WK, Nge O, Buntinx F, Muls E. [Albuminuria during the screening for diabetes in a semi-rural area (Kisantu City, DR Congo)]. *Nephrol Ther* 2010; 6: 513-519 [PMID: 20627763 DOI: 10.1016/j.nephro.2010.04.006]
- 36 Marshall SL, Edidin D, Sharma V, Ogle G, Arena VC, Orchard T. Current clinical status, glucose control, and complication rates of children and youth with type 1 diabetes in Rwanda. *Pediatr Diabetes* 2013; 14: 217-226 [PMID: 23279222 DOI: 10.1111/pedi.12007]
- 37 Motala AA, Pirie FJ, Gouws E, Amod A, Omar MA. Microvascular complications in South African patients with long-duration diabetes mellitus. *S Afr Med J* 2001; **91**: 987-992 [PMID: 11847923]
- 38 Nambuya AP, Otim MA, Whitehead H, Mulvany D, Kennedy R, Hadden DR. The presentation of newly-diagnosed diabetic patients in Uganda. *QJM* 1996; 89: 705-711 [PMID: 8917747]
- 39 Pruijm MT, Madeleine G, Riesen WF, Burnier M, Bovet P. Prevalence of microalbuminuria in the general population of Seychelles and strong association with diabetes and hypertension independent of renal markers. *J Hypertens* 2008; 26: 871-877 [PMID: 18398328 DOI: 10.1097/HJH.0b013e3282f624d9]
- 40 Rahlenbeck SI, Gebre-Yohannes A. Prevalence and epidemiology of micro- and macroalbuminuria in Ethiopian diabetic patients. J Diabetes Complications 1997; 11: 343-349 [PMID: 9365876]
- 41 Rasmussen JB, Thomsen JA, Rossing P, Parkinson S, Christensen DL, Bygbjerg IC. Diabetes mellitus, hypertension and albuminuria in rural Zambia: a hospital-based survey. *Trop Med Int Health* 2013; 18: 1080-1084 [PMID: 23763632 DOI: 10.1111/tmi.12139]
- 42 Rissassi JR, Nseka M, Jadoul M, Lepira FB, Mvitu M, Mbenza G, Yekoladio D, Aloni M, Nge OO. [Prevalence and determinants of microalbuminuria and macroalbuminuria in children and young adults with type 1 diabetes in Kinshasa]. *Nephrol Ther* 2010; 6: 40-46 [PMID: 19853548 DOI: 10.1016/j.nephro.2009.08.001]
- 43 **Rotchford AP**, Rotchford KM. Diabetes in rural South Africaan assessment of care and complications. *S Afr Med J* 2002; **92**: 536-541 [PMID: 12197196]
- 44 Sobngwi E, Mbanya JC, Moukouri EN, Ngu KB. Microalbuminuria and retinopathy in a diabetic population of Cameroon. *Diabetes Res Clin Pract* 1999; 44: 191-196 [PMID: 10462142]
- 45 **Wanjohi FW**, Otieno FC, Ogola EN, Amayo EO. Nephropathy in patients with recently diagnosed type 2 diabetes mellitus in black Africans. *East Afr Med J* 2002; **79**: 399-404 [PMID: 12638839]
- 46 **Worku D**, Hamza L, Woldemichael K. Patterns of diabetic complications at jimma university specialized hospital, southwest ethiopia. *Ethiop J Health Sci* 2010; **20**: 33-39 [PMID: 22434958]
- 47 Stanifer JW, Jing B, Tolan S, Helmke N, Mukerjee R, Naicker S, Patel U. The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Glob Health* 2014; 2: e174-e181 [PMID: 25102850 DOI: 10.1016/S2214-109X(14)70002-6]
- 48 Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline:

behind the scenes, need for guidance, and a framework for moving forward. *Kidney Int* 2014; **85**: 49-61 [PMID: 24284513 DOI: 10.1038/ki.2013.444]

- 49 National Collaborating Centre for Chronic Conditions. Chronic kidney disease: Early identification and management of chronic kidney disease in adults in primary and secondary care. London: NICE, 2008. Available from: URL: http://www.nice.org.uk/ nicemedia/live/12069/42117/42117.pdf
- 50 Swanepoel CR, Wearne N, Okpechi IG. Nephrology in Africa--not yet uhuru. *Nat Rev Nephrol* 2013; 9: 610-622 [PMID: 23958719 DOI: 10.1038/nrneph.2013.168]
- 51 Matsha TE, Yako YY, Rensburg MA, Hassan MS, Kengne AP, Erasmus RT. Chronic kidney diseases in mixed ancestry south African populations: prevalence, determinants and concordance between kidney function estimators. *BMC Nephrol* 2013; 14: 75 [PMID: 23547953 DOI: 10.1186/1471-2369-14-75]
- 52 Weil EJ, Curtis JM, Hanson RL, Knowler WC, Nelson RG. The impact of disadvantage on the development and progression of diabetic kidney disease. *Clin Nephrol* 2010; 74 Suppl 1: S32-S38 [PMID: 20979961]
- 53 Ruster C, Wolf G. The role of chemokines and chemokine receptors in diabetic nephropathy. *Front Biosci* 2008; 13: 944-955 [PMID: 17981602]
- 54 Iwano M, Plieth D, Danoff TM, Xue C, Okada H, Neilson EG. Evidence that fibroblasts derive from epithelium during tissue fibrosis. *J Clin Invest* 2002; 110: 341-350 [PMID: 12163453 DOI: 10.1172/JCI15518]

- 55 Seaquist ER, Goetz FC, Rich S, Barbosa J. Familial clustering of diabetic kidney disease. Evidence for genetic susceptibility to diabetic nephropathy. *N Engl J Med* 1989; **320**: 1161-1165 [PMID: 2710189 DOI: 10.1056/NEJM198905043201801]
- 56 Marre M, Jeunemaitre X, Gallois Y, Rodier M, Chatellier G, Sert C, Dusselier L, Kahal Z, Chaillous L, Halimi S, Muller A, Sackmann H, Bauduceau B, Bled F, Passa P, Alhenc-Gelas F. Contribution of genetic polymorphism in the renin-angiotensin system to the development of renal complications in insulin-dependent diabetes: Genetique de la Nephropathie Diabetique (GENEDIAB) study group. J Clin Invest 1997; 99: 1585-1595 [PMID: 9120002 DOI: 10.1172/JCI119321]
- 57 Nelson RG, Morgenstern H, Bennett PH. Intrauterine diabetes exposure and the risk of renal disease in diabetic Pima Indians. *Diabetes* 1998; 47: 1489-1493 [PMID: 9726239]
- 58 Zandi-Nejad K, Luyckx VA, Brenner BM. Adult hypertension and kidney disease: the role of fetal programming. *Hypertension* 2006; 47: 502-508 [PMID: 16415374 DOI: 10.1161/01.HYP.0000198544.099-09.1a]
- 59 Brancati FL, Whitle JC, Whelton PK, Seidler AJ, Klag MJ. The excess incidence of diabetic end-stage renal disease among blacks. A population-based study of potential explanatory factors. *JAMA* 1992; 268: 3079-3084 [PMID: 1433738]
- 60 Chaiken RL, Palmisano J, Norton ME, Banerji MA, Bard M, Sachimechi I, Behzadi H, Lebovitz HE. Interaction of hypertension and diabetes on renal function in black NIDDM subjects. *Kidney Int* 1995; 47: 1697-1702 [PMID: 7643539]

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