Diabetic nephropathy in Africa: A systematic review

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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.

**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[3,4], and communicable diseases such as invasive bacterial infections[5-8]. 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[9].

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[44]. 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
Table 1  Search history PubMed

| Search terms                                                                 | Hits  |
|------------------------------------------------------------------------------|-------|
| 1  Diabetes[tf] OR Diabetes mellitus[tf] OR Type 1 diabetes[mesh] OR Type 1 diabetes mellitus[tf] OR T1DM[tf] OR Type 2 diabetes[tf] | 445204|
| 2  Renal insufficiency[tf] OR Renal failure[tf] OR Renal injury[tf] OR Renal disease[tf] kidney insufficiency[tf] OR Kidney failure[tf] | 154354|
| 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] OR 54928 Burundi*[tw] OR Cameroon*[tw] OR 'Cape Verde'[tw] OR 'Central African Republic'[tw] OR Chad*[tw] OR Comoros*[tw] OR Congo*[tw] OR 'Democratic Republic of Congo'[tw] OR Djibouti*[tw] OR Egypt*[tw] OR 'Equatorial Guinea*[tw] OR Eritrea*[tw] OR Ethiopia*[tw] OR Gabon*[tw] OR Gambia*[tw] OR Ghana*[tw] OR Guinea*[tw] OR "Guinea Bissau"[tw] OR 'Ivory Coast'[tw] OR "Cote d'Ivoire"[tw] OR Jamahiriya*[tw] OR Jamahiriya*[tw] OR Kenya*[tw] OR Lesotho*[tw] OR Liberia*[tw] OR Libya*[tw] OR Libia*[tw] OR Madagascar*[tw] OR Malawi*[tw] OR Mali*[tw] OR Mauritania*[tw] OR Mauritius*[tw] OR Mayotte*[tw] OR Morocco*[tw] OR Mozambique*[tw] OR Mozambique*[tw] OR Namibia*[tw] OR Niger*[tw] OR Nigeria*[tw] OR Princip*[tw] OR Reunion*[tw] OR Rwanda*[tw] OR 'Sao Tome'[tw] OR Sao*[tw] OR Seychelles*[tw] OR 'Sierra Leone'[tw] OR Somalia*[tw] OR 'South Africa'[tw] OR 'St Helena'[tw] OR Sudan*[tw] OR Swaziland*[tw] OR Tanzania*[tw] OR Togo*[tw] OR Tunisia*[tw] OR Uganda*[tw] OR 'Western Sahara'[tw] OR Zaire*[tw] OR Zambia*[tw] OR Zimbabwe*[tw] OR 'Central African'[tw] OR 'Central African'[tw] OR 'West Africa'[tw] OR 'West African'[tw] OR 'Western Africa'[tw] OR 'Western African'[tw] OR 'East Africa'[tw] OR 'East African'[tw] OR 'Eastern African'[tw] OR 'Eastern African'[tw] OR 'North Africa'[tw] OR 'North African'[tw] OR 'Northern Africa'[tw] OR 'Southern Africa'[tw] OR 'South African'[tw] OR 'South African'[tw] OR 'sub Saharan Africa'[tw] OR 'sub Saharan Africa'[tw] OR 'sub Saharan Africa'[tw] OR 'sub Saharan Africa'[tw] OR 'sub Saharan African'[tw] NOT ('guinea pig'[tw] OR 'guinea pigs'[tw] OR 'aspergillus niger'[tw])))) | 1065  |
| 7  # 5 AND # 6                                                                 | 918   |
| 8  #4 Limits: 1994/01/01 to 2014/10/22 and studies done in Humans            |       |

| 918 articles retrieved from MEDLINE and screened based on title and abstract |
| 836 articles did not meet inclusion criteria                                 |
| 7 full-texts of potentially relevant articles were not found                 |
| 75 full-text articles assessed for eligibility                               |
| 6 articles from review of bibliographies                                     |
| 49 articles excluded                                                         |
| 32 articles included in the systematic review                                 |

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. Pruijm et al. in Seychelles in 2004, conducted a large-scale 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. 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). 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).

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. In another study in South Africa, found that 18.4% of T1DM patients had
| Ref. | Country     | Period                     | Design                                      | Setting | Sample size | Mean or median age (yr) | Male (%) | Type and duration of diabetes (yr) | Duration FUP | Method for CKD assessment          | Proteinuria                                      | MDRD | Urine ACR | Cockroft-Gault |
|------|-------------|----------------------------|---------------------------------------------|---------|-------------|-------------------------|----------|-----------------------------------|-------------|-----------------------------------|------------------------------------------------|------|-----------|----------------|
| Motala et al (37), 2001 | South Africa | Not precised              | Retrospective cohort study                  | Clinic, urban | 219         | 39.5 T1DM; 56.4 T2DM | 19.6     | 16.10 T1DM; 18.6 T2DM             | At least 10 yr | persistent proteinuria (Dipstick) | Proteinuria                                      |      |           |                |
| Elbagir et al (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)            | NA                                            |      |           |                |
| Sobngwi et al (44), 1999 | Cameroon     | Not precised              | Cross-sectional, self-selected sampling    | Clinic, urban | 64          | 37.4 normotensive T1DM; 51.7 normotensive T2DM; 57.9 hypertensive T1DM | 35.7     | Proteinuria                      | NA                                            |      |           |                |
| Motala et al (37), 2001 | South Africa | Not precised              | Retrospective cohort study                  | Clinic, urban | 219         | 39.5 T1DM; 56.4 T2DM | 19.6     | 16.10 T1DM; 18.6 T2DM             | At least 10 yr | persistent proteinuria (Dipstick) | Proteinuria                                      |      |           |                |
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| Sobngwi et al (44), 1999 | Cameroon     | Not precised              | Cross-sectional, self-selected sampling    | Clinic, urban | 64          | 37.4 normotensive T1DM; 51.7 normotensive T2DM; 57.9 hypertensive T1DM | 35.7     | Proteinuria                      | NA                                            |      |           |                |

**Note:** Table 2: General characteristics of studies of chronic kidney disease in people with diabetes in Africa.
| Study                                                                 | Country | Year        | Sampling Type                      | Study Design             | Site                     | N   | Age | Sex | T1DM | T2DM | Proteinuria Type | Proteinuria Unit |
|----------------------------------------------------------------------|---------|-------------|------------------------------------|--------------------------|--------------------------|-----|-----|-----|------|------|------------------|------------------|
| Rotchford et al[40], 2002                                             | South Africa | 1999       | Cross-sectional, self-selected sampling | Clinic, rural           | South Africa             | 253 | 56.5| 26.9| 42.2 | T1DM and T2DM | NA               | Urine ACR        |
| Risasi et al[40], 2009                                               | DR Congo | 11 June 2008 to 30 July 2008 | Cross-sectional, self-selected sampling | Clinic, urban             | DR Congo                 | 181 | 19.1| 38.7| 57.6 | T1DM | NA               | Urine ACR        |
| Rahlenbeck et al[43], 1997                                            | Ethiopia | January - April 1995  | Cross-sectional, self-selected sampling | Clinic, urban             | Ethiopia                 | 170 | 31.4| 53.7| 10.3 | T2DM | NA               | Proteinuria      |
| Wanjohi et al[43], 2002                                               | Kenya   | June 2000 - January 2001 | Cross-sectional, self-selected sampling | Clinic, urban             | Kenya                    | 100 | 53.7| 37  | 10.3 | T2DM | NA               | Albuminuria      |
| Nambuya et al[38], 1996                                               | Uganda  | 1 January 1993 - 10 August 1994 | Cross-sectional, self-selected sampling | Clinic, urban/urban (origin of participants) | Uganda                  | 252 | Not precised | 46.4 | 45 (range 30-69) | T2DM and T1DM | NA               | Proteinuria      |
| Rissassi et al[42], 2009                                              | DR Congo | 11 June 2008 to 30 July 2008 | Cross-sectional, self-selected sampling | Clinic, urban             | DR Congo                 | 181 | 19.1| 38.7| 57.6 | T1DM | NA               | Urine ACR        |
| Rahlenbeck et al[40], 1997                                            | Ethiopia | January - April 1995  | Cross-sectional, self-selected sampling | Clinic, urban             | Ethiopia                 | 170 | 31.4| 53.7| 10.3 | T2DM | NA               | Proteinuria      |
| Wanjohi et al[43], 2002                                               | Kenya   | June 2000 - January 2001 | Cross-sectional, self-selected sampling | Clinic, urban             | Kenya                    | 100 | 53.7| 37  | 10.3 | T2DM | NA               | Albuminuria      |
| Nambuya et al[38], 1996                                               | Uganda  | 1 January 1993 - 10 August 1994 | Cross-sectional, self-selected sampling | Clinic, urban/urban (origin of participants) | Uganda                  | 252 | Not precised | 46.4 | 45 (range 30-69) | T2DM and T1DM | NA               | Proteinuria      |
| Rissassi et al[42], 2009                                              | DR Congo | 11 June 2008 to 30 July 2008 | Cross-sectional, self-selected sampling | Clinic, urban             | DR Congo                 | 181 | 19.1| 38.7| 57.6 | T1DM | NA               | Urine ACR        |
| Rahlenbeck et al[40], 1997                                            | Ethiopia | January - April 1995  | Cross-sectional, self-selected sampling | Clinic, urban             | Ethiopia                 | 170 | 31.4| 53.7| 10.3 | T2DM | NA               | Proteinuria      |
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| Nambuya et al[38], 1996                                               | Uganda  | 1 January 1993 - 10 August 1994 | Cross-sectional, self-selected sampling | Clinic, urban/urban (origin of participants) | Uganda                  | 252 | Not precised | 46.4 | 45 (range 30-69) | T2DM and T1DM | NA               | Proteinuria      |
| Rissassi et al[42], 2009                                              | DR Congo | 11 June 2008 to 30 July 2008 | Cross-sectional, self-selected sampling | Clinic, urban             | DR Congo                 | 181 | 19.1| 38.7| 57.6 | T1DM | NA               | Urine ACR        |
| Rahlenbeck et al[40], 1997                                            | Ethiopia | January - April 1995  | Cross-sectional, self-selected sampling | Clinic, urban             | Ethiopia                 | 170 | 31.4| 53.7| 10.3 | T2DM | NA               | Proteinuria      |
| Wanjohi et al[43], 2002                                               | Kenya   | June 2000 - January 2001 | Cross-sectional, self-selected sampling | Clinic, urban             | Kenya                    | 100 | 53.7| 37  | 10.3 | T2DM | NA               | Albuminuria      |
| Nambuya et al[38], 1996                                               | Uganda  | 1 January 1993 - 10 August 1994 | Cross-sectional, self-selected sampling | Clinic, urban/urban (origin of participants) | Uganda                  | 252 | Not precised | 46.4 | 45 (range 30-69) | T2DM and T1DM | NA               | Proteinuria      |

ACR: Albumin-to-Creatinine Ratio; FUP: Follow-up; MDRD: Modification of diet renal disease; NA: Not applicable.
| Ref.                | Country          | Sample size | Type of diabetes | Duration of follow-up | Diagnostic criteria for CKD                                                                 | Prevalence | Incidence | Comments                                                                 |
|--------------------|------------------|-------------|------------------|-----------------------|---------------------------------------------------------------------------------------------|-------------|------------|--------------------------------------------------------------------------|
| Motala et al[37], 2001 | South Africa     | 219         | T1DM and T2DM    | 16.10 (4.9) yr        | Persistent proteinuria (dipstick 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 et al[44], 1999 | Cameroon         | 64          | T1DM and T2DM    | Not applicable        | MDRD: CKD stage ≥ 2 according to the National Kidney foundation                             | 53.1%       | Not applicable          |                                                                          |
| Katchinga et al[43], 2010 | DR Congo        | 98          | T2DM             | Not applicable        | Proteinuria (30 mg/24 h)                                                                    | 18.1%       | Not applicable          |                                                                          |
| Choukem et al[22], 2012 | Cameroon         | 420         | T2DM             | Not applicable        | Microalbuminuria: Urine Albumin-to-Creatinine Ratio 3.4-33.9 mg albumin/mmol creatinine     | 31%         | Not applicable          |                                                                          |
| Keeton et al[41], 2004 | South Africa     | 59          | T2DM             | 12 yr                 | Urine Albumin-to-Creatinine Ratio (no detail)                                                | Not applicable |                        | 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 and in 66.1% (39/59) the SCR level had doubled during the study |
| Pruijn et al[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[34], 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 et al[15], 2014 | Nigeria          | 65          | T2DM             | Not applicable        | MDRD: eGFR ≤ 60 mL/min per 1.73 m²                                                            | 43.1%       | Not applicable          |                                                                          |
| Levitt et al[35], 1997 | South Africa     | 243         | T2DM and T1DM    | Not applicable        | Urine Albumin-to-Creatinine Ratio > 3.4 mm/mmol Persistent proteinuria (for at least 3 consecutive visits) | 36.7%       | Not applicable          |                                                                          |
| Majaliwa et al[44], 2007 | Tanzania        | 99          | T1DM             | Not applicable        | Proteinuria (no detail)                                                                     | 29.3%       | Not applicable          |                                                                          |
| Marshall et al[35], 2013 | Rwanda           | 286         | T1DM             | Not applicable        | Microalbuminuria: Urine Albumin-to-Creatinine Ratio = 30-299 mg/g                           | Microalbuminuria: 21%; Microalbuminuria: 5% | Not applicable |                                                                          |
| Alebiosu et al[36], 2003 | Nigeria          | 465         | T2DM             | Not applicable        | Proteinuria and eGFR                                                                       | 41.1%       | Not applicable          | The method for the estimation of the GFR is not indicated Death due to chronic renal failure after 20 yr of follow-up was 9/49 (after exclusion of lost to follow) |
| Gill et al[38], 2005   | South Africa     | 88          | T1DM             | 20 yr                 | Persistent dipstick proteinuria                                                              | Not applicable |                        | Death of renal cause after 20 yr = 18.4% (9/49)                                                                          |
| Djojolo et al[35], 2001 | Benin            | 152         | T1DM and T2DM    | Not applicable        | Proteinuria (no detail)                                                                     | 20%         | Not applicable          |                                                                          |
| Rotchford et al[35], 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          |                                                                          |
| Study | Country | Number | Type | Not applicable | Microalbuminuria: Urine Albumin-to-Creatinine Ratio = 30-299 mg/g | Macroalbuminuria: Urine Albumin-to-Creatinine Ratio ≥ 300 mg/g | T1DM: 21.9% (microalbuminuria) and 7.3% (macroalbuminuria) | Not applicable |
|-------|---------|--------|------|----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|----------------|
| Rissassi et al[42], 2009 | DR congo | 181 | T1DM | Not applicable | Microalbuminuria: > 30 mg/L | Macroalbuminuria: > 300 mg/L | T1DM: 32% (microalbuminuria) and 15% (macroalbuminuria) | Not applicable |
| Rahlenbeck et al[40], 1997 | Ethiopia | 170 | T1DM and T2DM | Not applicable | Microalbuminuria: > 30 mg/L | Macroalbuminuria: > 300 mg/L | T1DM: 21.9% (microalbuminuria) and 7.3% (macroalbuminuria) | Not applicable |
| Wanjohi et al[45], 2002 | Kenya | 100 | T2DM | Not applicable | Proteinuria ≥ 20 mg | 26% | Not applicable |
| Nambuya et al[38], 1996 | Uganda | 252 | T1DM and T2DM | Not applicable | Proteinuria (no detail) | 17.1% | Not applicable |
| Rasmussen et al[81], 2013 | Ethiopia | 101 | T1DM and T2DM | Not applicable | Microalbuminuria: ACR > 3.5-35.0 for women and 2.5-25.0 mg/mmol for men | Microalbuminuria: > 300 mg/g | Microalbuminuria: 23.8% | Not applicable |
| Bentata et al[19], 2013 | Morocco | 72 | T1DM | 5 yr | At the time of enrollement | Microalbuminuria: 36.1% | Nephropathy: 15.3% | Microalbuminuria: 91% |
| Gill et al[27], 2008 | Ethiopia | 105 | T1DM and T2DM | Not applicable | Nephropathy: ACR > 25.0 mg/mmol and retinopathy present | Microalbuminuria: 51% | Urinary ACR levels (to assess microalbuminuria and nephropathy) were done on admission were repeated on three specimens at three-monthly intervals |
| Bouzid et al[81], 2011 | Tunisia | 689 | T2DM | Not applicable | CKD: eGFR < 60 mL/min per 1.73 m² (Cockroft-Gault) | Microalbuminuria: 13% | Microalbuminuria: 10.1% | Not applicable |
| Janmohamed et al[81], 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 proteinuria | CKD: 19.8% | Microalbuminuria: 2% | Microalbuminuria: 30% |
| Danquah et al[81], 2012 | Ghana | 671 | T2DM | Not applicable | Proteinuria ≥ 20 mg/L | 43% | Not applicable |
| Lutale et al[81], 2007 | Tanzania | 244 | T1DM and T2DM | Not applicable | Microalbuminuria: AER 20-200 μg/min | Microalbuminuria: 12.1% (T1DM); 9.8% (T2DM) | Microalbuminuria: 1.1% (T1DM); 7.2% (T2DM) | Not applicable |

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Microalbuminuria:
- Urine Albumin-to-Creatinine Ratio = 30-299 mg/g
- Urine Albumin-to-Creatinine Ratio ≥ 300 mg/g

Macroalbuminuria:
- Urine Albumin-to-Creatinine Ratio > 300 mg/g

Proteinuria:
- > 20 mg/L

Microalbuminuria:
- ACR > 2.5 and < 25.0 mg/mmol in men and > 3.5 and < 25.0 mg/mmol in women

Macroalbuminuria:
- AER ≥ 200 μg/min

CKD:
- eGFR < 60 mL/min per 1.73 m² (Cockroft-Gault)

Renal failure:
- eGFR < 60 mL/min per 1.73 m² (MDRD)

Nephropathy:
- ACR > 25.0 mg/mmol and retinopathy present

Overt proteinuria:
- eGFR < 60 mL/min per 1.73 m²: 24.7%

Macroalbuminuria was significantly associated with CKD (P < 0.00001).
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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, and obesity. 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. 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, 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. 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) increase in the risk of nephropathy. 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). 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.

DISCUSSION

Diabetic nephropathy is a common and morbid complication 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 follow-up. Diagnosed duration of diabetes, blood pressure variables, advancing age, obesity and to some extent 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. This review identified 90 articles representing data from 21 countries, with over half of the studies originating from South Africa, Nigeria and Ethiopia alone. 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. 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
| Ref. | Country | Sample size | Type of diabetes | Diagnostic criteria for CKD | Risk factor | Measure of association | Factors adjusted for | Comments |
|------|---------|-------------|------------------|-----------------------------|-------------|------------------------|----------------------|----------|
| Motala et al[37], 2001 | South Africa | 219 | T1DM and T2DM | Persistent proteinuria | Not assessed | | | |
| Elbagir et al[26], 1995 | Sudan | 128 | Insulin-treated | Proteinuria | | | | |
| Sobongwi et al[44], 1999 | Cameroon | 64 | T1DM and T2DM | Proteinuria | | | | |
| Katshunga et al[30], 2010 | DR Congo | 98 | T2DM | Proteinuria | | | | |
| Choukem et al[22], 2012 | Cameroon | 420 | T2DM | Proteinuria (50 mg/24 h) | | | | |
| Keeton et al[31], 2004 | South Africa | 59 | T2DM | Urine Albumin-to-Creatinine Ratio (no detail) | | | | |
| Pruijm et al[39], 2008 | Seychelles | 1218 | All types | Microalbuminuria: Urine Albumin-to-Creatinine Ratio 3.4-33.9 mg albumin/mmol creatinine | Not assessed | | | |
| Akebi et al[16], 2003 | Nigeria | 342 | T1DM and T2DM | Persistent proteinuria | Not assessed | | | |
| Bouaziz et al[32], 2012 | Tunisia | 73 | T2DM | Microalbuminuria: < 2.8 g/mol for women and < 2.5 g/mol for men | | | | |
| Ajayi et al[15], 2014 | Nigeria | 65 | T2DM | MDRD: eGFR ≤ 60 mL/min per 1.73 m² | Not assessed | | | |
| Levitt et al[33], 1997 | South Africa | 243 | T2DM and T1DM | Urine Albumin-to-Creatinine Ratio > 3.4 mm/mmol and Persistent proteinuria (for at least 3 consecutive visits) | Not assessed | | | |

**Table 4: Risk factors for chronic kidney disease in people with diabetes**

| Ref. | Country | Sample size | Type of diabetes | Diagnostic criteria for CKD | Risk factor | Measure of association | Factors adjusted for | Comments |
|------|---------|-------------|------------------|-----------------------------|-------------|------------------------|----------------------|----------|
| Motala et al[37], 2001 | South Africa | 219 | T1DM and T2DM | Persistent proteinuria | Not assessed | | | |
| Elbagir et al[26], 1995 | Sudan | 128 | Insulin-treated | Proteinuria | | | | |
| Sobongwi et al[44], 1999 | Cameroon | 64 | T1DM and T2DM | Proteinuria | | | | |
| Katshunga et al[30], 2010 | DR Congo | 98 | T2DM | Proteinuria | | | | |
| Choukem et al[22], 2012 | Cameroon | 420 | T2DM | Proteinuria (50 mg/24 h) | | | | |
| Keeton et al[31], 2004 | South Africa | 59 | T2DM | Urine Albumin-to-Creatinine Ratio (no detail) | | | | |
| Pruijm et al[39], 2008 | Seychelles | 1218 | All types | Microalbuminuria: Urine Albumin-to-Creatinine Ratio 3.4-33.9 mg albumin/mmol creatinine | Not assessed | | | |
| Akebi et al[16], 2003 | Nigeria | 342 | T1DM and T2DM | Persistent proteinuria | Not assessed | | | |
| Bouaziz et al[32], 2012 | Tunisia | 73 | T2DM | Microalbuminuria: < 2.8 g/mol for women and < 2.5 g/mol for men | | | | |
| Ajayi et al[15], 2014 | Nigeria | 65 | T2DM | MDRD: eGFR ≤ 60 mL/min per 1.73 m² | Not assessed | | | |
| Levitt et al[33], 1997 | South Africa | 243 | T2DM and T1DM | Urine Albumin-to-Creatinine Ratio > 3.4 mm/mmol and Persistent proteinuria (for at least 3 consecutive visits) | Not assessed | | | |
### Table: Diabetic Nephropathy in Africa

| Study | Country | Sample Size | Type of DM | Proteinuria | Risk Factors | OR (95% CI) | P-value |
|-------|---------|-------------|------------|-------------|-------------|-------------|---------|
| Majaliwa et al. [34], 2007 | Tanzania | 99 | T1DM | Proteinuria (no detail) | Missing insulin doses | | P = 0.045 | Not available |
| Marshall et al. [35], 2013 | Rwanda | 286 | T1DM | Microalbuminuria: Urine Albumin-to-Creatinine Ratio = 30-299 mg/g | Duration of diabetes (one year increase) | aOR: 0.86, 95%CI: 0.77-0.96 | P = 0.009 | Each variable is adjusted for the others |
| | | | | | Age (increase) | aOR: 0.86, 95%CI: 0.77-0.96 | P = 0.008 | |
| | | | | | Diastolic BP (increase) | aOR: 0.86, 95%CI: 0.77-0.96 | P = 0.004 | |
| | | | | | HBA1c (increase) | aOR: 0.86, 95%CI: 0.77-0.96 | P = 0.047 | |
| Alebiosu et al. [36], 2003 | Nigeria | 465 | T2DM | Proteinuria and eGFR (no detail) | Hypertension, left ventricular hypertrophy, stroke and myocardial infarction were more frequent in advanced stages of nephropathy | Not available | P < 0.05 | Not available |
| | | | | | Duration of diabetes (one year increase) | aOR: 0.86, 95%CI: 0.77-0.96 | P = 0.008 | |
| | | | | | Diastolic BP (increase) | aOR: 0.86, 95%CI: 0.77-0.96 | P = 0.004 | |
| | | | | | HBA1c (increase) | aOR: 0.86, 95%CI: 0.77-0.96 | P = 0.047 | |
| Gill et al. [37], 2005 | South Africa | 88 | T1DM | Persistent dipstick proteinuria | | | Not available | Not available |
| Djoko et al. [38], 2001 | Benin | 152 | T1DM and T2DM | Proteinuria (no detail) | | | Not available | Not available |
| | | | | | Duration of diabetes > 5 yr | | < 0.001 | Model contains duration of diabetes, BMI, HbA1c, age and hypertension |
| Rotchford et al. [39], 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 | 4.19 (1.93-9.10) | < 0.001 | |
| | | | | | BMI > 33 | 0.27 (0.08-0.48) | 0.002 | |
| | | | | | HbA1c > 14% | 4.69 (1.65-13.3) | 0.004 | |
| | | | | | Hypertension | 2.11 (1.07-4.17) | 0.031 | |
| | | | | | Age > 18 yr | 2.9 (1.3-6.2) | No precision | |
| | | | | | HbA1c > 10% | 2.6 (1.6-4) | No precision | |
| Rshallbeck et al. [40], 1997 | Ethiopia | 170 | T1DM and T2DM | Microalbuminuria: Urine Albumin-to-Creatinine Ratio ≥ 0.3 mg/g | Duration of diabetes | Beta = 0.061, SE = 0.018 for T1DM | < 0.001 | Hypertensive patients excluded |
| | | | | | albuminuria > 0.3 mg/L | Systolic blood pressure | Beta = 0.018 for T1DM | |
| | | | | | | None identified | Beta = 0.027, SE = 0.008 for T1DM | |
| | | | | | | None assessed | |
| Wanjohi et al. [41], 2002 | Kenya | 100 | T2DM | Proteinuria ≥ 20mg | | | None identified | |
| Nambya et al. [42], 1996 | Uganda | 252 | T1DM and T2DM | Proteinuria (no detail) | | | None assessed | |
| Rasmussen et al. [43], 2013 | Zambia | 101 | T1DM and T2DM | Microalbuminuria: ACR = 3.5-35.0 for women and 2.5-25.0 mg/mmol for men | | | None assessed | |
| | | | | | Macroalbuminuria were ACR > 35.0 for women and > 25.0 for men | | | |
| Bentata et al. [44], 2013 | Maroc | 72 | T1DM | End-stage renal disease: eGFR < 15 mL/min | Hemoglobin blood (per 1 g/dL decrease) | 3.18 (1.47-6.87) | 0.003 | No precision |
| | | | | | Diastolic blood pressure (per 1 mmHg increase) | 1.15 (1.04-1.27) | 0.006 | |

Majaliwa et al. [34], 2007
Marshall et al. [35], 2013
Alebiosu et al. [36], 2003
Gill et al. [37], 2005
Djoko et al. [38], 2001
Rotchford et al. [39], 2002
Rissassi et al. [40], 2009
Rahlebeck et al. [41], 1997
Wanjohi et al. [42], 2002
Nambya et al. [43], 1996
Rasmussen et al. [44], 2013
Bentata et al. [45], 2013

These are independent risk factors for ESRD in type-1 diabetes patients with diabetic nephropathy.
| Study | Country | Participants | Diagnosis | Renal Involvement | Diabetes Outcomes | Other Predictors | Measure of Association | p-Value | Results |
|-------|---------|--------------|-----------|------------------|------------------|-----------------|----------------------|--------|---------|
| Gill et al. [27], 2008 | Ethiopia | 105 | T1DM and T2DM | Nephropathy: ACR > 25.0 mg/mmol and retinopathy present | None assessed | | | | |
| | | | Microalbuminuria: ACR > 2.5 and < 25.0 mg/mmol in men and > 3.5 and < 25.0 mg/mmol in women | | | | | |
| Bouzid et al. [21], 2011 | Tunisia | 689 | T2DM | Renal failure: creatinine clearance < 60 mL/min (Cockroft-Gault) | Microalbuminuria: ACR > 2.5 and < 25.0 mg/mmol in men and > 3.5 and < 25.0 mg/mmol in women | Older age | Not provided | < 0.0001 | < 0.0001 |
| | | | | | | Hypertension | | 0.01 | 0.01 |
| | | | | | | Long duration of diabetes | | 0.02 | 0.02 |
| | | | | | | Higher BMI | | 0.03 | 0.03 |
| Janmohamed et al. [29], 2013 | Tanzania | 369 | T1DM and T2DM | CKD: eGFR < 60 mL/min per 1.73 m² (Cockroft-Gault) or microalbuminuria (> 20 mg/L) or overt proteinuria | | Older age | 1.03 (1.00-1.05) | 0.05 | Adjustment made, but no precision |
| Danquah et al. [23], 2012 | Ghana | 671 | T2DM | Proteinuria ≥ 20 mg/l | | | | | |
| | | | | | | Duration of diabetes | 0.090 (0.049-0.131) | 0.03 | 0.03 |
| Lutale et al. [33], 2007 | Tanzania | 244 | T1DM and T2DM | Abnormal proteinuria: AER > 20 μg/min | | | | | |
| Worku et al. [46], 2010 | Ethiopia | 305 | T1DM and T2DM | Proteinuria (no detail) | | | | | |
| Makulo et al. [35], 2010 | DR Congo | 81 | No precision | Microalbuminuria: ACR 30-299 mg/g | | | | | |
| | | | | | | Macroalbuminuria: ACR ≥ 300 mg/g | | | |
| | | | | | | Renal failure: eGFR < 60 mL/min per 1.73 m² | | | |
| Eghan et al. [25], 2007 | Ghana | 109 | T1DM and T2DM | Microalbuminuria: ACR 30-300 mg/g | | | | | |
| | | | | | | Duration of diabetes | 0.04 | | The associations were assessed by comparing patients with and without microalbuminuria |
| | | | | | | Serum creatinine | 0.05 | 0.05 |
| | | | | | | Blood urea nitrogen | 0.01 | 0.01 |
| | | | | | | Urine potassium | 0.0061 | 0.0061 |
| | | | | | | Duration of diabetes | < 0.05 | 0.05 |
| | | | | | | Serum total cholesterol | < 0.05 | 0.05 |
| | | | | | | Alcohol > 30 mg/d | < 0.05 | 0.05 |
| | | | | | | Peripheral vascular disease | < 0.05 | 0.05 |
| | | | | | | Stroke | < 0.05 | 0.05 |

CKD: Chronic kidney disease; BMI: Body mass index; ACR: Albumin-to-Creatinine Ratio; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus; eGFR: Epidermal growth factor receptor.
more frequent in population with diabetes within Africa than in developed countries. The review by Stanifer et al\cite{1} 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\cite{2}. 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\cite{3}. 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\cite{4} 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\cite{5}; 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\cite{6}, 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\cite{6}.

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\cite{7}. Other hallmarks of diabetic nephropathy include nodular diabetic glomerulosclerosis and diffuse glomerulosclerosis, mediated at least in part by inflammatory processes and immune cells activity\cite{8}. 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\cite{9}.

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 polygenic. 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\cite{10}. Some studies have suggested some detrimental effect of the double-deletion (DD) polymorphism of the angiotensin-converting enzyme (ACE) genotype on disease progression\cite{11}. Non-genetic determinants of diabetic nephropathy include among others socioeconomic factors, dietary factors, poor hyperglycemic control, hypertension, obesity and early life factors\cite{12,13}. Hypertension appears to be a strong correlate of disease progression in Black people\cite{14,15}.

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.
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 of 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.

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