European Journal of Medical and Health Sciences
Vol 6 | Issue 6 | December 2024
ISSN 2593-8339

RESEARCH ARTICLE

Characteristics and Risk of Incident Diabetic Nephropathy between Early-onset versus Late-onset Type 2 Diabetics of Nigerian Origin

Collins Amadi[1,2,*], Johnbosco Chidozie Okafor[3], Ochuko Otokunefor[2,4], and Ezra Agbo[5]

ABSTRACT

Background: **Diabetic nephropathy (DN), the most common complication of type 2 diabetes (T2DM), has been reported to occur more often among the early-onset type 2 diabetes (ET2DM) compared to the late-onset type 2 diabetes (LT2DM) in the Western populations with no previous data on this subject in Nigeria. Hence, the current study evaluated the incidence and risk of DN between ET2DM versus LT2DM.**

Methods: **This was a retrospectively designed cross-sectional observational study conducted at the Rivers State University Teaching Hospital, Southern Nigeria. Socio-demographic, anthropometric, clinical, and laboratory data for 10 years (2014–2023) were obtained from medical records of T2DM patients with similar DM duration and analyzed using descriptive/inferential statistics.**

Results: **During the studied period, 3,111 adults were diagnosed with T2DM of which 352 (11.3%) presented with incident DN. T2DM cohorts with incident DN were mostly those with ET2DM diagnosis (n = 218; 61.9%) compared to the LT2DM. The ET2DM cohorts were relatively younger with higher proportions of positive DM family history, overweight/obesity status, blood pressure, plasma creatinine/glucose, urine albumin-to-creatinine ratio, and HbA1c but lower eGFR at presentation than the LT2DM cohorts. The ET2DM was significantly associated with incident DN following crude (HR: 6.986; 95%CI: 3.476–9.518; p < 0.001) and confounder-adjusted (HR: 4.684; 95%CI: 2.270–7.114; p < 0.001) Cox proportional regression models compared to the LT2DM cohorts.**

Conclusion: **DN is common among patients with T2DM and more particularly prevalent among younger patients with metabolic condition. Hence, aggressive exploration of renal status should be made mandatory during the initial evaluation of T2DM among younger patients.**

Keywords: Diabetic nephropathy, early-onset 2 diabetes, type 2 diabetes.

Submitted: August 14, 2024

Published: December 03, 2024

10.24018/ejmed.2024.6.6.2182

[1]Department of Chemical Pathology, Rivers State University, Nigeria.
[2]Department of Chemical Pathology, PAMO University of Medical Sciences, Nigeria.
[3]Department of Chemical Pathology, University of Uyo Teaching Hospital, Nigeria.
[4]Department of Chemical Pathology, University of Port Harcourt, Nigeria.
[5]Department of Chemical Pathology, University of Uyo Teaching Hospital, Nigeria.

**Corresponding Author:*
e-mail: collins338@yahoo.com

1. Introduction

It has become common knowledge and an established scientific fact that the current global pattern of type 2 diabetes mellitus (T2DM) has assumed an obvious pandemic dimension [1], [2]. This current dimension is majorly steered by the global obesity epidemic, including inactive lifestyle choices among those at risk [1]–[3]. Based on this current epidemiologic trajectory, it has been predicted to be more catastrophic for low- and middle-income countries in the next few decades [3].

T2DM is characterized by various complications that arise insidiously during the disease [4]. These complications are employed in establishing the disease prognostic dynamics [3], [4]. Consequently, diabetic nephropathy (DN) has been recognized as the most common complication of T2DM [5]. DN, which is a major determinant and cause of DM-related morbidity and mortality, has been widely documented to be highly common among patients with T2DM [5].

Current epidemiologic data indicate that DN tends to occur and progresses rapidly among patients with early-onset T2DM (ET2DM) compared to those with later-onset T2DM (LT2DM) [6]. This portends significant clinical, social, economic, and public health consequences for those with ET2DM [6]–[9]. However, most of these previous epidemiologic data have emanated from Western populations and remain yet to be verified among Nigerians.

Hence, the current study evaluated the characteristics and risk of DN among patients with newly diagnosed ET2DM versus newly diagnosed LT2DM at the Rivers State University Teaching Hospital, Southern Nigeria.

2. Materials and Methods

2.1. Design, Setting, and Site

This descriptive, cross-sectional, and retrospective study was conducted at the Rivers State University Teaching Hospital (RSUTH) in Rivers State, Southern Nigeria. RSUTH is one of the Nigeria federal government-affiliated tertiary health institutions in River State which is a major referral health institution in the state.

2.2. Ethical Considerations

The ethical approval of the study was obtained from the Research Ethics Committee of RSUTH. The study was thereafter conducted by the core basic principles encapsulated in the Helsinki Declaration.

2.3. Tools and Target Populations

The study was carried out using only the relevant anonymized medical data, obtained at initial presentation and at diagnosis in RSUTH, from all the eligible T2DM-diagnosed population in RSUTH before the initiation of any form of medical intervention among the study population.

2.4. Data Acquisition

The relevant data was obtained from the medical records of all eligible study population, using a well-structured data extraction template, by trained research assistants. All the data were acquired at the point of initial T2DM diagnosis and included the followings: age, sex, educational level, residential area, occupational status, family history of diabetes (DM), alcohol/cigarette consumption status, duration of classic T2DM symptoms before diagnosis, T2DM duration, blood pressure, body mass index (BMI), and all initial relevant laboratory parameters such as fasting plasma glucose (FPG), random plasma glucose (RPG), glycated hemoglobin A1c (HbA1c), serum electrolytes (sodium, potassium, chloride, bicarbonate), urea, creatinine, urine protein, hematuria, and urine albumin to creatinine ratio (UACR).

2.5. Eligibility Criteria

The criteria for inclusion were as follows:

1. Medical records of all T2DM patients diagnosed with incident adult-onset (≥18 but <65 years of age) T2DM in RSUTH over 10 years (January 2014 to the 31st of December 2023).
2. Medical records of all T2DM patients who had similar duration (6–7 months) of the classic symptoms (frequent urination, polyphagia, and polydipsia plus or minus unintended weight loss, fatigue, poor wound healing, poor vision, and frequent genito-urinary infections) of T2DM before presenting in RSUTH.
3. Medical records of those enjoying relatively good health without any other pre-existing/existing comorbidities before the onset of the classic T2DM symptoms.

The criteria for exclusion were as follows:

1. Medical records of those aged <18 years and >65 years of age,
2. Medical records of those with any other class of DM,
3. Medical records of those presenting with incident acute/chronic complications of T2DM
4. Medical records of pregnant patients,
5. Medical records of those with any pre-existing/existing comorbidities or on drugs that can alter renal function/urine protein excretion (ACE inhibitors, etc) at presentation,
6. Medical records of those diagnosed outside RSUTH before presentation in RSUTH,
7. Medical records of those with incomplete relevant study data.

2.6. Laboratory Protocols

During the study period, all specimen collection and laboratory protocols were carried out following standardized guidelines. Plasma electrolytes (sodium, potassium, chloride, and bicarbonate) were determined on ion-selective electrode automated electrolyte analyzer (SFRI 6000, Medical Diagnostics, Bordeaux France).

FPG, RPG, urea, and creatinine were determined on an automated chemistry analyzer (BS200, Mindray, China). Glycated hemoglobin AIc (HbA1c) was determined via ion-exchange chromatography (D10, Biorad Diagnostics, USA). Urine chemistry analyses was done on an automated urine analyzer (Combilyzer-13, Human Diagnostics Worldwide, Wiesbaden, Germany).

2.7. Laboratory Diagnosis

During the study period, T2DM diagnosis was based on both the 1999 World Health Association (WHO) and the 2010 American Diabetes Association (ADA) diagnostic criteria as previously described [10].

1. The T2DM diagnosis was based on the 1999 WHO guideline if one or more of the following laboratory parameters was met among any suspected case in the presence of the classic symptoms:
   a) FPG ≥7.0 mmol/l,
   b) RPG ≥11.1 mmol/l,
   c) Two-hour OGTT ≥11.1 mmol/l.

2. Based on the 2010 ADA criteria, T2DM was diagnosed when the HbA1c level exceeds 6.5% among

any suspected case in the presence of the classic symptoms.

2.8. *Definitions/Categorization of Study Variables*

1. T2DM diagnosis was defined based on meeting the following characteristics:
   a) No history of being on insulin therapy since diagnosis,
   b) Being on, and responsive to, oral anti-hyperglycemic medications since diagnosis,
   c) Nil history or evidence of type 1 diabetes autoimmune markers.
2. BMI obtained from weight in meters divided by square of height in meters was stratified as underweight (<18.5), normal (18.5–24.9), overweight (25–29.9), or obese (≥30).
3. Those presenting with incident T2DM at age ≤40 years excluding secondary DM (drug- or chemical-induced, exocrine pancreas disease, genetic defects), MODY, gestational diabetes and rare forms of diabetes were designated as having ET2DM and those presenting at age >40 years were designated as having LT2DM.
4. DN positive was defined based on the following clinical/laboratory characteristics as previously described [11]:
   a) Persistent UACR of >30 mg/mmol, determined in fasting spot urine specimen, that was confirmed on at least 2 of 3 specimens collected during a 3–6 months period.
   b) Plus/minus progressive decline in the estimated glomerular filtration rate (eGFR).
   c) Presence of diabetic retinopathy.
   d) Elevated arterial blood pressure (>130/80 mmHg).
   e) Absence of clinical/laboratory evidence of any other renal or urinary tract diseases.
5. The eGFR was calculated using the MDRD formula and expressed in milliliters per minute [12].

2.9. *Data Processing and Analysis*

Data was managed using the SPSS v23 for Windows (IBM Corp., Armonk, NY, USA). The non-categorical variables were summarized using means/standard deviations and compared using the Student t test or analysis of variance, when appropriate. Categorical variables were summarized using proportions expressed as numbers/frequencies; between-group comparisons were determined using the Chi-squared test. The Cox proportional hazards model was used to define the association of DN among the categories of studied cohorts. The Schoenfeld residuals test was used to check the proportional hazard model assumption. Hazard ratios with its respective 95% confidence intervals were reported to show significance and strength of association. A two-tailed test was used to evaluate statistical significance, and a probability value (p-value) of <0.05 was considered statistically significant.

3. Results

During the studied period (2014–2024), 3,111 adults were diagnosed with incident T2DM as depicted in Table I. Of that total, 352 (11.3%) presented with varied clinical and laboratory characteristics consistent with incident DN (Table I). Those who presented with the incident DN were relatively younger and had higher systolic and diastolic blood pressure compared to those who presented without the incident DN ($p < 0.05$; Table I). Additionally, those with the incident DN were majorly those who presented with early-onset T2DM (n = 218; 61.9%) compared to those who presented with late-onset T2DM (n = 134; 38.1%) ($p < 0.05$; Table I).

Those who presented with the early-onset T2DM were relatively younger, had higher proportions of positive family history of DM, higher overweight/obesity status, and higher mean systolic and diastolic blood pressure compared to the late-onset T2DM cohorts ($p < 0.05$; Table II).

Moreover, those who presented with early-onset T2DM also had higher plasma creatinine, FPG, RPG, UACR, and HbA1c but lower eGFR at presentation compared to those with the late-onset T2DM ($p < 0.05$; Table III).

Compared to the late-onset T2DM cohorts, the early-onset T2DM cohorts had a significant association with incident diabetic nephropathy following crude (HR: 6.986; 95% CI: 3.476–9.518; $p < 0.001$) and adjusted (HR: 4.684; 95% CI: 2.270–7.114; $p<0.001$) Cox proportional regression analyses (Table IV).

4. Discussion

4.1. *Major Findings*

During the study period, 3,111 adults were diagnosed with T2DM of which 352 (11.3%) presented with incident DN. T2DM cohorts with incident DN were mostly those with ET2DM diagnosis (n = 218; 61.9%) compared to the LT2DM. The ET2DM cohorts were relatively younger with higher proportions of DM family history, overweight/obesity status, systolic/diastolic blood pressure, plasma creatinine/glucose, urine albumin-to-creatinine ratio, and HbA1c but lower eGFR at presentation compared to the LT2DM cohorts. The ET2DM cohorts also had a higher risk of incident DN following crude and confounder-adjusted Cox proportional regression analyses compared to the LT2DM cohorts.

4.2. *Relationship of Findings with Existing Literature*

The incidence rate of DN observed in the current study among the studied cohorts is relatively high and seems to align with the incidence rate documented in a similar retrospective study conducted in Ethiopia [13]. The high incidence rate may also reflect the rising incidence of type 2 diabetes within the studied area [10]. In contrast, the incidence rate of DN documented in the current study is lower than those reported in Middle Eastern Countries [14]. The variance in these documented incident rates may be related to differences in study design and population characteristics of those sampled in these previous studies.

Recent studies evaluating diabetic complications, including DN, in early-onset versus later-onset type 2 diabetes

TABLE I: Baseline Features of Enrolled Study Population (n = 3,110)

Variables	All DM cohorts	DN positive	DN negative	p-value
	Mean ± SD/n (%)	Mean ± SD/n (%)	Mean ± SD/n (%)	**DN+ vs DN-**
N	3,110 (100)	352 (11.3)	2,758 (88.7)	<0.001*
Time of T2DM onset				<0.001*
ET2DM	644 (20.7)	218 (61.9)	426 (15.5)	
LT2DM	2,467 (79.3)	134 (38.1)	2,333 (84.5)	
Mean age, years	57.32 ± 7.88	46.91 ± 5.66	56.93 ± 8.47	<0.001*
Gender				0.328
Male	1,501 (48.3)	175 (49.7)	1,326 (48.1)	
Female	1,609 (51.7)	177 (50.3)	1,432 (51.9)	
Residential area				0.414
Urban	1,557 (50.1)	173 (49.2)	1,384 (50.2)	
Rural	1,553 (49.9)	179 (50.8)	1,374 (49.8)	
Family history of DM				0.424
Yes	1,513 (48.6)	174 (49.4)	1,339 (48.5)	
No	1,597 (51.4)	178 (50.6)	1,419 (51.5)	
Educational level				0.117
Primary	154 (5.0)	16 (4.4)	138 (5.0)	
Secondary	1,220 (39.2)	120 (34.1)	1,100 (40.0)	
Tertiary	1,736 (55.8)	206 (58.5)	1,530 (55.0)	
Occupation				0.166
Civil servant	1,185 (38.1)	139 (39.5)	1,046 (38.0)	
Farmer	113 (3.7)	11 (3.1)	102 (3.7)	
Self-employed	1,033 (33.2)	167 (47.4)	866 (31.4)	
Retired	445 (14.3)	15 (4.3)	430 (15.6)	
Student/others	334 (10.7)	20 (5.7)	314 (11.3)	
Alcohol intake				0.255
Yes	626 (20.1)	75 (21.3)	551 (20.0)	
No	2,484 (79.9)	277 (78.7)	2,207 (80.0)	
Cigarette smoking				0.143
Yes	308 (9.9)	37 (10.5)	271 (9.8)	
No	2,802 (90.1)	315 (89.5)	2,487 (90.2)	
BMI status				0.220
Normal	667 (21.5)	97 (27.6)	570 (20.7)	
Overweight	1,534 (49.3)	132 (37.5)	1,402 (50.8)	
Obese	909 (29.2)	123 (34.9)	786 (28.5)	
Blood pressure, mmHg				
Systolic	129.44 ± 8.67	136.57 ± 8.08	125.79 ± 8.16	<0.001*
Diastolic	78.59 ± 5.33	83.44 ± 4.32	74.91 ± 4.22	<0.001*
Duration of DM symptoms before presentation, days	191.13 ± 13.66	190.45 ± 13.80	191.02 ± 13.14	0.414

Note: *Statistically significant; DM: Diabetes mellitus; DN: Diabetic nephropathy; SD: Standard deviation; BMI: Body mass index; DM: Diabetes mellitus.

have vastly documented these complications to be more pronounced among the early-onset cases compared to the later-onset cases [6]–[9]. Early-onset T2DM has also been reported as a risk factor for DN progression in a recent biopsy-based study [6]. This observation is supported by the findings in the current study, where most early-onset cases presented with DN compared to the later-onset cases. The present observation is further strengthened by the higher risk of DN documented among the early-onset type 2 diabetics compared to the later-onset type 2 diabetics in the current study.

Furthermore, the early-onset cohorts were also observed to have a higher preponderance of family history of DM, overweight/obesity status, blood pressure, plasma creatinine/glucose, urine albumin-to-creatinine ratio, and HbA1c but lower eGFR at presentation/diagnosis. These are clinical/laboratory parameters that have been documented in association with the severity and aggressive metabolic dynamics of T2DM with co-existent DN among the early-onset type 2 diabetics in previous studies [6]–[9], [15], [16].

4.3. Mechanism of DN in Early-onset T2DM

The mechanisms of DN in early-onset type 2 diabetics relative to later-onset type 2 diabetics remain speculative in the literature. However, most observational and experimental reports have dwelled on the severity and aggressive nature of the T2DM dynamics to explain the preponderance of DN and other complications in early-onset T2DM [17]–[20]. Accelerated decline in beta cell function and severe insulin resistance have been suggested to play major

TABLE II: Baseline Features by Diabetic Nephropathy Status and Time of T2DM Onset

Variables	All DN cohorts	ET2DM	LT2DM	p-value
	Mean ± SD/n (%)	Mean ± SD/n (%)	Mean ± SD/n (%)	**ET2DM VS. LT2DM**
N	352 (100)	218 (61.9)	134 (38.1)	
Time of T2DM onset	46.91 ± 5.66	36.88 ± 5.09	58.68 ± 7.33	<0.001*
ET2DM				0.064
LT2DM	175 (49.7)	107 (49.1)	68 (50.7)	
Mean age, years	177 (50.3)	111 (50.9)	66 (49.9)	
Gender				0.300
Male	173 (49.2)	108 (49.5)	65 (47.5)	
Female	179 (50.8)	110 (50.5)	69 (52.5)	
Residential area				0.023*
Urban	174 (49.4)	123 (56.4)	51 (38.1)	
Rural	178 (50.6)	95 (43.6)	83 (61.9)	
Family history of DM				0.116
Yes	16 (4.4)	10 (4.6)	6 (4.5)	
No	120 (34.1)	61 (28.0)	59 (44.0)	
Educational level	206 (58.5)	137 (67.4)	69 (51.5)	
Primary				0.204
Secondary	139 (39.5)	85 (40.0)	54 (40.3)	
Tertiary	11 (3.1)	7 (3.2)	4 (3.0)	
Occupation	167 (47.4)	100 (45.9)	67 (50.0)	
Civil servant	15 (4.3)	11 (5.0)	4 (3.0)	
Farmer	20 (5.7)	15 (6.9)	5 (3.7)	
Self-employed				0.166
Retired	75 (21.3)	49 (22.8)	26 (19.4)	
Student/others	277 (78.7)	159 (87.2)	118 (80.6)	
Alcohol intake				0.098
Yes	37 (10.5)	15 (6.9)	22 (16.6)	
No	315 (89.5)	203 (93.1)	112 (83.4)	
Cigarette smoking				0.014*
Yes	97 (27.6)	30 (13.8)	67 (50.0)	
No	132 (37.5)	101 (46.3)	31 (33.5)	
BMI status	123 (34.9)	87 (39.9)	36 (16.5)	
Normal				
Overweight	136.57 ± 8.08	138.44 ± 7.96	127.65 ± 7.40	<0.001*
Obese	83.44 ± 4.32	87.51 ± 4.63	83.33 ± 4.48	0.022*
Blood pressure, mmHg	190.45 ± 13.80	189.71 ± 13.45	190.76 ± 13.44	0.378

Note: *Statistically significant; SD: Standard deviation; DN: Diabetic nephropathy; ET2DM: Early onset type 2 diabetes; LT2DM: Late onset type 2 diabetes; BMI: Body mass index; DM: Diabetes mellitus.

TABLE III: Laboratory Features by Diabetic Nephropathy Status and by Time of T2DM Onset

	Diabetic nephropathy cohorts			
Parameters	**All DN cohorts**	**ET2DM**	**LT2DM**	**p-value ET2DM vs LT2DM**
N	352	218	134	
	Mean ± SD/n (%)	Mean ± SD/n (%)	Mean ± SD/n (%)	
Plasma sodium, mmol/L	138.74 ± 9.78	136.66 ± 9.77	135.49 ± 9.76	0.304
Plasma potassium, mmol/L	3.57 ± 1.13	3.66 ± 1.15	3.57 ± 1.14	0.122
Plasma chloride, mmol/L	96.78 ± 6.55	96.70 ± 6.57	95.76 ± 6.56	0.267
Plasma bicarbonate, mmol/L	28.67 ± 3.70	26.62 ± 3.17	28.65 ± 3.20	0.089
Plasma urea, mmol/L	4.68 ± 1.18	4.87 ± 1.16	4.34 ± 4.26	0.174
Plasma creatinine, µmo/L	121.41 ± 5.52	126.77 ± 5.72	97.45 ± 5.31	<0.001*
eGFR, mls/minute	92.35 ± 7.14	76.79 ± 7.22	95.67 ± 7.61	<0.001*
FPG, mmol/L (n = 152)	8.66 ± 2.05	9.21 ± 2.34	8.11 ± 2.21	0.002*
RPG, mmol/L (n = 200)	12.54 ± 3.29	13.88 ± 3.47	12.04 ± 3.30	0.014*
HbA1c, %	8.86 ± 2.01	10.67 ± 2.22	9.94 ± 2.81	0.165
UACR, mg/mmol	39.35 ± 3.41	47.92 ± 3.55	37.37 ± 3.42	<0.001*

Note: *Statistically significant; DN: Diabetic nephropathy; SD: Standard deviation; ET2DM: Early onset type 2 diabetes; LT2DM: Late onset type 2 diabetes; FPG: Fasting plasma glucose; RPG: Random plasma glucose; HbA1c: Glycated hemoglobin A1c; UACR: Urine albumin to creatinine ratio.

TABLE IV: Risk of Incident Diabetes Nephropathy among the ET2DM and LT2DM Study Populations

T2DM onset time	Unadjusted HR	95% CI; p-value	Adjusted HR**	95% CI; p-value
LT2DM	1.0 (Reference)	—	1.0 (Reference)	—
ET2DM	6.986	3.476–9.518; <0.001	4.684	2.270–7.114; <0.001*

Note: *Statistically significant; ET2DM: Early onset type 2 diabetes; LT2DM: Late onset type 2 diabetes; SD: Standard deviation; HR: Hazard ratio; CI: Confidence interval; **Adjusted for age, family history of diabetes mellitus, BMI, systolic/diastolic blood pressure, plasma creatinine, estimated glomerular filtration rate, fasting/random plasma glucose, and urine albumin to creatinine ratio.

roles in the severity and aggressiveness of T2DM in early-onset T2DM [16]. Compared to the later-onset T2DM cohorts and despite having a similar duration of T2DM in the current study, the early-onset T2DM cohorts had worse glycemic status and higher systolic/diastolic blood pressures. These are factors associated with a decline in beta cell function and enhanced insulin resistance, respectively, which tend to heighten the risk of incident DN in early-onset T2DM [6]–[9].

4.4. Relevance of Findings to Clinical Practice and Future Research

The study findings indicate the need to aggressively pursue the evaluation of renal status as early as possible in early-onset T2DM cohorts at presentation and diagnosis. Furthermore, future research should be structured to reveal the exact mechanisms underlying the incidence of DN in early-onset T2DM.

4.5. Strengths and Limitations of the Current Study

The study's strength lies in the use of a relatively large sample size population who are all newly diagnosed and treatment-naïve T2DM cases at the acquisition of the relevant data for analysis. However, our data should be interpreted in the context of several limitations. First, as the natural history of T2DM is quite a complex one, we could only deduce the age they were diagnosed with T2DM rather than the exact onset time of T2DM. Secondly, we could not exclude all other possible confounding factors for the natural complexity of DN in T2DM. Thirdly, because of the difficulty of laboratory differential diagnosis, other DM types may be misdiagnosed as T2DM in the current study. Notwithstanding these limitations, our study offers valuable insights into the characteristics of DN in a Nigerian population.

5. Conclusion

In conclusion, although with the comparable T2DM duration, patients with early-onset T2DM had a higher proportion and risk of DN than those with later-onset T2DM. This calls for urgent attention to the evaluation of patients with early-onset T2DM. Hence, the study's findings emphasize the need for aggressive exploration of renal status, which should be made mandatory during the initial evaluation among younger patients with T2DM.

Acknowledgment

The authors appreciate all the efforts of the resident doctors for professional assistance during conduct of the study.

Ethics Statement

The study protocol was approved by the Institutional Research Ethics Committee (approval reference number 2023/282).

Author Contributions

All the authors were involved substantially in the concept and design of the study, acquisition, analysis, and interpretation of the data, drafting the article, revising the article critically for its intellectual content, and in the final approval of the version to be published.

Conflict of Interest

The authors have no conflict of interest to declare.

References

[1] Reed J, Bain S, Kanamarlapudi V. A review of current trends with type 2 diabetes epidemiology, aetiology, pathogenesis, treatments and future perspectives. *Diabetes Metab Syndr Obes*. 2021;14:3567–602. doi: 10.2147/DMSO.S319895.

[2] Beulens JWJ, Pinho MGM, Abreu TC, den Braver NR, Lam TM, Huss A, *et al.* Environmental risk factors of type 2 diabetes-an exposome approach. *Diabetologia*. 2022;65(2):263–74. doi: 10.1007/s00125-021-05618-w.

[3] Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, *et al.* IDF diabetes atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183:109119.

[4] Mansour A, Mousa M, Abdelmannan D, Tay G, Hassoun A, Alsafar H. Microvascular and macrovascular complications of type 2 diabetes mellitus: exome wide association analyses. *Front Endocr (Lausanne)*. 2023;14:1143067. doi: 10.3389/fendo.2023.1143067.

[5] Hu Q, Chen Y, Deng X, Li Y, Ma X, Zeng J, *et al.* Diabetic nephropathy: focusing on pathological signals, clinical treatment, and dietary regulation. *Biomed Pharmacother*. 2023;159:114252. doi: 10.1016/j.biopha.2023.114252.

[6] Wu Y, Wang Y, Zhang J, Zhang R, Zhao L, Ren H, *et al.* Early-onset of type 2 diabetes mellitus is a risk factor for diabetic nephropathy progression: a biopsy-based study. *Aging (Albany NY)*. 2021;13(6):8146–54. doi: 10.18632/aging.202624.

[7] Liu JJ, Liu S, Gurung RL, Ang K, Tang WE, Sum CF, *et al.* Risk of progressive chronic kidney disease in individuals with early-onset type 2 diabetes: a prospective cohort study. *Nephrol Dial Transplant*. 2020;35(1):115–21. doi: 10.1093/ndt/gfy211.

[8] Yu R, Liu X, Li R, Xiao X. Ten-year clinical characteristics of patients with early-onset type 2 diabetes: a single-center experience in China. *J Diabetes*. 2023;1–9. doi: 10.1111/1753-0407.13477.

[9] Cho Y, Park HS, Huh BW, Seo SH, Seo DH, Ahn SH, *et al.* Prevalence and risk of diabetic complications in young-onset versus late-onset type 2 diabetes mellitus. *Diabetes Metab*. 2022;48(6):101389.
[10] Amadi C, Onung S, Ayoade O, Abudu E, Unyime F, Usoro A. The incident pattern and trend of type 2 diabetes among adults in Akwa Ibom State, South-South Nigeria. *Int J Diabetes Endocrinol*. 2021;4(4):142–9.
[11] Persson F, Rossing P. Diagnosis of diabetic kidney disease: state of the art and future perspective. *Kidney Int Suppl (2011)*. 2018 Jan;8(1):2–7. doi: 10.1016/j.kisu.2017.10.003.
[12] Imai E, Horio M, Nitta K, Yamagata K, Iseki K, Tsukamoto Y *et al.* Modification of the modification of diet in renal disease (MDRD) study equation for Japan. *Am J Kidney Dis*. 2007;50(6):927–37.
[13] Kebede SA, Tusa BS, Weldesenbet AB, Tessema ZT, Ayele TA. Incidence of diabetic nephropathy and its predictors among type 2 diabetes mellitus patients at university of gondar comprehensive Specialized Hospital, Northwest Ethiopia. *J Nutr Metab*. 2021;2021:6757916.
[14] Aldukhayel A. Prevalence of diabetic nephropathy among type 2 diabetic patients in some of the Arab countries. *Int J Health Sci (Qassim)*. 2017;11(1):1–4.
[15] Solis-Herrera C, Triplitt CL, Lynch JL. Nephropathy in youth and young adults with type 2 diabetes. *Curr Diab Rep*. 2014;14(2):456. doi: 10.1007/s11892-013-0456-y.
[16] Lascar N, Brown J, Pattison H, Barnett AH, Bailey CJ, Bellary S. Type 2 diabetes in adolescents and young adults. *Lancet Diabetes Endocrinol*. 2018;6(1):69–80.
[17] Amatruda M, Gembillo G, Giuffrida AE, Santoro D, Conti G. The aggressive diabetic kidney disease in youth-onset type 2 diabetes: pathogenetic mechanisms and potential therapies. *Medicina (Kaunas)*. 2021;57(9):868. doi: 10.3390/medicina57090868.
[18] Liu Y, Huang H, Gao R, Liu Y. Dynamic phenotypes and molecular mechanisms to understand the pathogenesis of diabetic nephropathy in two widely used animal models of Type 2 Diabetes Mellitus. *Front Cell Dev Biol*. 2020;8:172. doi: 10.3389/fcell.2020.00172.
[19] Karalliedde J, Gnudi L. Diabetes mellitus, a complex and heterogeneous disease, and the role of insulin resistance as a determinant of diabetic kidney disease. *Nephrol Dial Transplant*. 2016;31(2): 206–13.
[20] Jung CY, Yoo TH. Pathophysiologic mechanisms and potential biomarkers in diabetic kidney disease. *Diabetes Metab J*. 2022;46(2):181–97.