BMC Nephrology

RESEARCH

Open Access

Decline in eGFR and mortality among type II diabetic patients: a 3-year prospective cohort study from Palestine

Mohammad Jaber[1†], Anas Sharabati[1†], Khaled Nofal[1†], Mohanad Hassan[2], Zakaria Hamdan[2*] and Zaher Nazzal[3*]

Abstract

Introduction Diabetic nephropathy is a significant complication of diabetes and a leading cause of chronic kidney disease (CKD) globally. This study aimed to assess the decline of renal function and all-cause mortality and identify the contributing risk factors among Palestinian patients with diabetes.

Methodology The study employed a prospective cohort design, enrolling 311 patients with type 2 diabetes mellitus (T2DM) attending primary health care centers in Palestine. Baseline data were collected in 2018 to determine the prevalence of CKD in patients with T2DM. Subsequently, the patients were followed up for three years to assess renal function and identify significant associated risk factors. The primary outcomes examined were estimated glomerular filtration rate (eGFR) decline and all-cause mortality.

Results During the three-year follow-up, 37.5% of the patients experienced eGFR decline, averaging 4.2 ml/min/1.73 m^2 per year. Males showed a significant association with eGFR decline with 5 times higher risk of developing eGFR decline. Hypertensive patients were 2.4 times more likely to experience decline. Regarding all-cause mortality, 14.1% of the patients died, with an incidence rate of 51.3 deaths per 1000 person-years. The risk of all-cause mortality was 5.5 times greater for patients with impaired renal function at baseline and 10.8 times greater for patients who had eGFR decline.

Conclusion This study highlights the importance of early detection of CKD in patients with diabetes, prompting more comprehensive management of risk factors related to eGFR decline and mortality. Furthermore, it underscores the need for future research in this patient population, including investigations about other relevant risk factors and the impact of different medications, such as anti-diabetic and antihypertensive medications, on the GFR decline and mortality rate.

Keywords Diabetes, Diabetic nephropathy, eGFR decline, Mortality, Palestine

†Mohammad Jaber, Anas Sharabati and Khaled Nofal contributed equally to this research.

*Correspondence:
Zakaria Hamdan
z.hamdan@najah.edu
Zaher Nazzal
znazzal@najah.edu

[1]Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine
[2]Internal Medicine, Internal Medicine Department, An-Najah National University Hospital, Nablus, Palestine
[3]Community Medicine, Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine

Introduction

Diabetic nephropathy is a major cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide [1, 2]. All patients with T2DM should have an annual screening for diabetic nephropathy, which includes measuring estimated glomerular filtration rate (eGFR) and urine albumin levels [3]. eGFR, which considers factors like age, race, and gender, is the primary method for assessing kidney function. CKD is defined as having eGFR < 60 or eGFR ≥ 60 ml/min/1.73 m^2 with evidence of kidney damage, such as albuminuria, according to KDIGO 2012 guidelines [4].

Kidney function naturally declines with age, with a gradual decrease in eGFR in persons aged 70 and above [5]. However, the decline in eGFR in patients with CKD is influenced by a variety of factors, several of which are modifiable, such as hypertension, elevated blood sugar levels, smoking, dietary habits, and obesity [6]. Identifying and controlling these risk factors is crucial to delay the onset and progression of kidney disease.

Over 15 years, a UK study revealed that 38% of patients with diabetes developed albuminuria, 28% developed renal impairment, and 14% developed both conditions [7]. The progression of CKD in patients with diabetes is an inevitable process. In the early stages of diabetic nephropathy, hyper-filtration occurs, leading to an increase in eGFR. As the disease progresses, eGFR decreases, and patients ultimately develop ESRD [8]. CKD significantly raises the risk of all-cause mortality in patients with diabetes, increasing it from 11.5% for those with diabetes alone to 31.1% for those with both diabetes and CKD [9, 10].

The decline in eGFR in CKD patients is linked to significant healthcare costs, with costs increasing dramatically as kidney function deteriorates. For example, the cost of care ranges from a few hundred dollars per month for individuals with mild CKD to tens of thousands of dollars per month for patients in advanced stages or ESRD [11, 12]. These financial implications further underscore the importance of early intervention and targeted management strategies.

In Palestine, the prevalence of diabetes mellitus in the West Bank was 15.3% in 2010 and is forecast to increase to 23.4% in 2030 [13, 14]. In 2019, a study conducted in Gaza revealed that 45.2% of adults aged 40 and older who regularly visited primary healthcare centers were diagnosed with type 2 diabetes [15]. In addition, diabetes was the fourth leading cause of death, accounting for 12.1% of all deaths in 2019 versus 8.9% in 2014 [16–18]. This study builds upon a previous cross-sectional baseline study undertaken by the research team back in 2018, aimed to determine the prevalence of CKD among diabetic adults, revealing a rate of 23.6% [19]. The primary objective of the current study is to assess the three-year decline in renal function and mortality in the previous study's cohort of patients with diabetes and identify key associated risk factors. The findings will contribute to a better understanding of eGFR decline in this population and help guide healthcare strategies to reduce mortality and improve the quality of care for patients with diabetes in the region.

Methodology

Study design and data source

This study employed a prospective cohort design, enrolling patients with T2DM who sought care at primary healthcare (PHC) clinics in various cities in the North West Bank region. In Palestine, individuals diagnosed with diabetes are registered in PHC centers, where they undergo regular monitoring and receive comprehensive healthcare treatment. This study serves as a follow-up to prior research conducted in 2018, referred to as the baseline study [19]. In 2018, we collected baseline data, encompassing information related to hypertension, creatinine levels, HbA1c measurements, and other pertinent variables, from T2DM patients receiving treatment at PHC centers in the North West Bank region. In the current study, we initiated a three-year follow-up starting in 2018, evaluating the decline of kidney function and monitoring other variables that could potentially influence kidney function and all-cause mortality. All patients who participated in the baseline study were included in the current study except those who were alive and had lost follow-up beyond 2018. Data collection took place between September 2018 and March 2022, utilizing electronic medical records and patient files from the PHC centers. The data was securely stored, ensuring restricted access solely to researchers involved in the project. The necessary approvals were received from the An-Najah National University Institutional Review Board (Reference #: Med. Sep. 2021/8) and the Ministry of Health.

Measurements and laboratory data

For this study, hypertension status, smoking history, HbA1c, and lipid profile, including HDL and LDL cholesterol, were extracted from patients' computerized records. The blood pressure measurements were taken by skilled nurses utilizing electronic sphygmomanometers and were subsequently documented in the records. Height and weight measurements were retrieved from patients' medical records and employed to calculate body mass index (BMI). Obesity was determined as a BMI ≥ 30.

Creatinine readings for each year were obtained from medical records, and the 2009 CKD-Epi formula was utilized to calculate eGFR [20, 21]. We used the 2009 version to ensure consistency with the baseline study for comparative analysis. Impaired renal function (IRF) was defined as eGFR < 60 ml/min/1.73 m^2.

The study's primary outcomes encompassed eGFR decline and all-cause mortality status. eGFR decline was defined as a decrease in eGFR after a three-year follow-up, calculated by subtracting the latest eGFR reading from the 2018 baseline reading. All-cause mortality was defined as individuals who died during the follow-up period.

Statistical analysis

Statistical analyses were conducted using SPSS version 20.0 for Windows software (IBM Corp., Armonk, NY). Categorical data were expressed as counts and percentages, while continuous data were presented as mean ± standard deviation unless specified otherwise. Differences in patient characteristics and risk factors of eGFR decline and mortality were assessed using the chi-square test for categorical variables and the independent t-test for continuous variables when appropriate. Multivariate binary logistic regression was employed to control for confounders and assess variables associated with eGFR decline and mortality. Statistical significance was defined as a p-value < 0.05.

Results

Out of the initial pool of 386 patients, 311 participants were included in the current study, as 75 patients were excluded due to loss of follow-up and incomplete records. At baseline, the average age of the sample was 61 ± 10.1 years, and the mean BMI was 32.8 ± 5.8. Among the participants, 51.1% were female, and 31.8% identified as smokers. Moreover, 79.8% of the participants also had hypertension, with an average duration of 8.9 ± 7.6 years. All study subjects had diabetes, with an average duration of 12.4 ± 8.2 years. The mean eGFR level was 73.7 ± 23.9. Additionally, 73% of the patients had eGFR ≥ 60 (Table 1).

Table 1 Clinical, background, and laboratory characteristics of the participants ($n = 311$)

Variables	Baseline *n* (%)
Age in years*(Mean ± SD)*	61 ± 10.1
Gender	
Male	152 (48.9%)
Female	159 (51.1%)
Smoker	96 (31.8%)
BMI*(Mean ± SD)*	32.8 ± 5.8
HTN	241 (79.8%)
HTN Duration in years*(Mean ± SD)*	8.9 ± 7.6
DM Duration in years*(Mean ± SD)*	12.4 ± 8.2
eGFR*(Mean ± SD)*	73.7 ± 23.9
eGFR level*(ml/min/1.73 m²)*	
≥ 90	89 (28.6%)
60–89	138 (44.4%)
< 60	84 (27%)

After a 3-year follow-up, 37.5% ($n = 108$) of patients exhibited eGFR decline. Among those, the mean eGFR decline over the three years was 12.47 ml/min/1.73 m², equivalent to approximately 4.2 ml/min/1.73 m² per year. In terms of all-cause mortality, 14.1% ($n = 44$; 95%CI: 10.5–18.5%) of patients died with an incidence rate of 51.3 deaths per 1000 person-years (Fig. 1). We classified patients into five groups according to their eGFR at 3-year follow-up and found that groups with eGFR ≥ 60 had a higher mean eGFR at 3-year follow-up than baseline. Conversely, groups with eGFR < 60 exhibited a lower mean eGFR at 3-year follow-up than baseline (Fig. 2). We also classified patients according to their eGFR at baseline. As patients' baseline eGFR decreased, the mortality rate increased. Individuals without IRF (eGFR ≥ 60) had 24.4 deaths per 1000 person-years, while those with IRF (eGFR < 60) had 92.5 deaths per 1000 person-years (Fig. 3).

Table 2 displays the patients' background characteristics and clinical and laboratory predictors related to the eGFR decline. Notably, the average age of patients with eGFR decline was 63.1 years, which was higher than the average age of those without decline (59.3 years) ($p = 0.002$). Regarding gender, approximately 56% of male patients experienced eGFR decline, while 21.1% of females did ($p < 0.001$). Among hypertensive patients, 41.9% had eGFR decline, compared to 19% among those without hypertension ($p < 0.001$). There was a significant association between IRF at baseline (eGFR < 60) and eGFR decline ($p = 0.013$). Around 50% of patients with IRF at baseline developed eGFR decline, whereas only 33.5% of patients without IRF at baseline did. However, it is important to note that the mean values for BMI, duration of both diabetes and hypertension, smoking status, HbA1c, HDL and LDL cholesterol levels did not have a significant impact on eGFR decline. Multivariate regression analysis showed that gender (aP-value < 0.001; aOR: 5; 95%CI: 2.7–8.9) and hypertension (aP-value = 0.033; aOR: 2.4; 95%CI: 1.1–5.2) increase the odds of eGFR decline.

We investigated the factors associated with all-cause mortality (Table 3). Our findings revealed that patients who died had a higher average age at baseline (64.4 years) compared to those who were still alive (60.4 years) ($p = 0.014$). Furthermore, there was a significant difference in mortality between males (19.1%) and females (9.4%) ($p = 0.015$). Regarding hypertension, 15.4% of patients with hypertension died, while only 8.2% of those without hypertension died ($p = 0.149$). When examining the eGFR at baseline, we observed that deceased patients had a lower mean baseline eGFR of 55.7 (± 26.4) ml/min/1.73 m2, whereas surviving patients had a higher mean baseline eGFR of 76.6 (± 22.2) ml/min/1.73 m2 ($p < 0.001$). Additionally, 32.1% of patients with IRF at

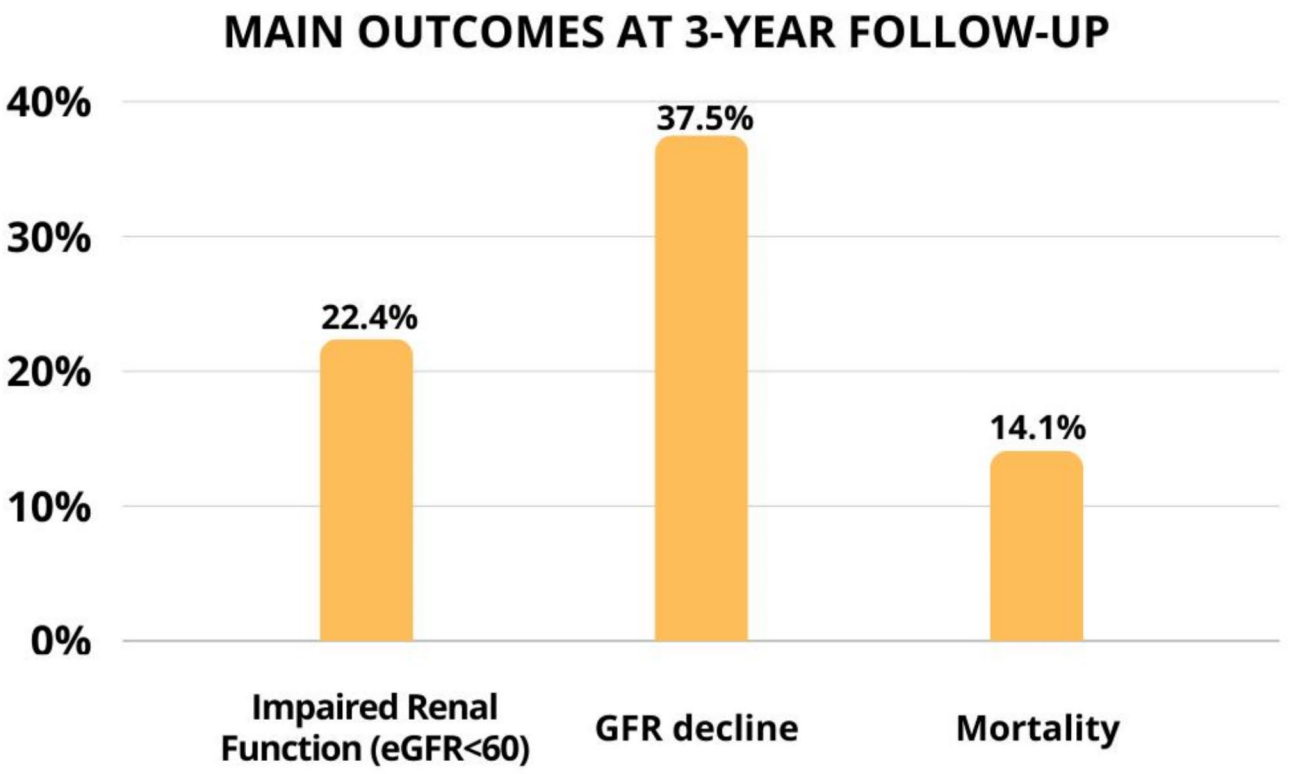

Fig. 1 Diabetic patients' outcomes after 3-year follow-up

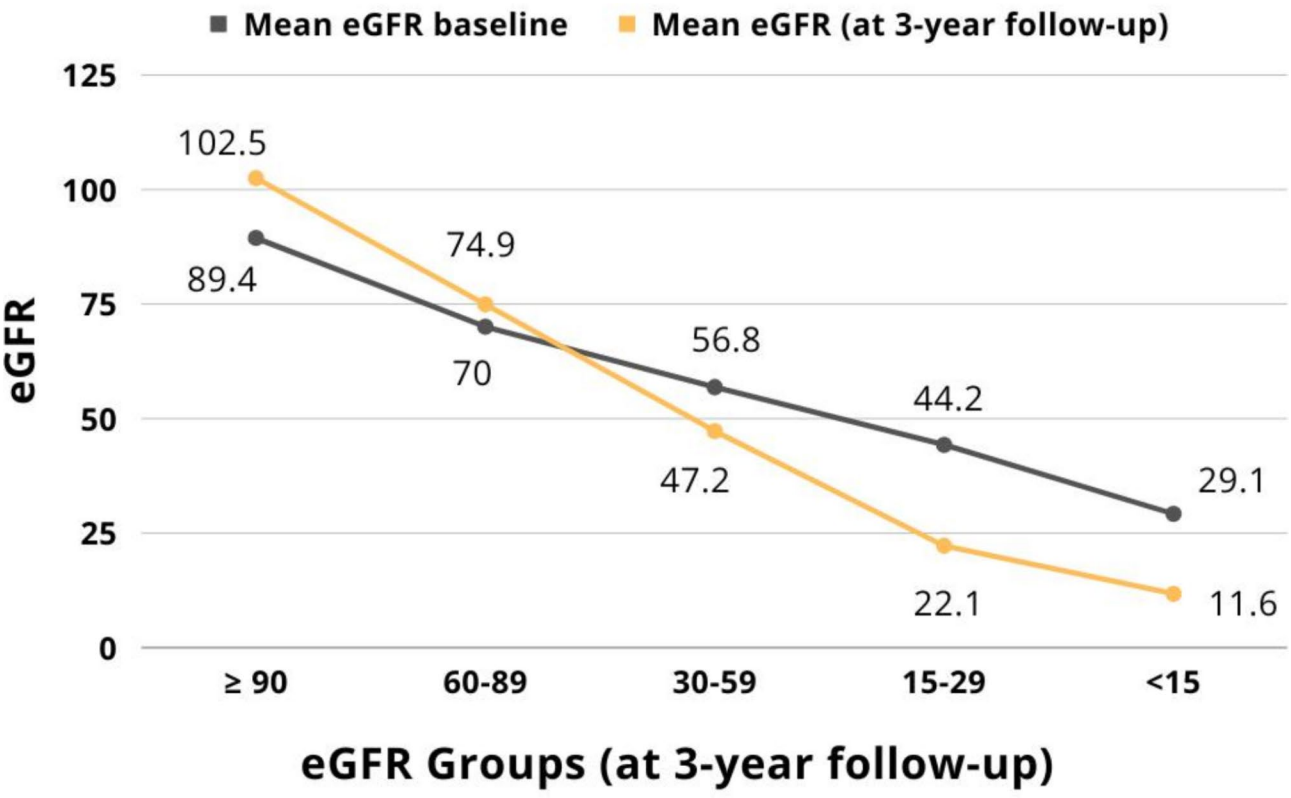

Fig. 2 Mean eGFR changes over 3-year follow-up for each eGFR group

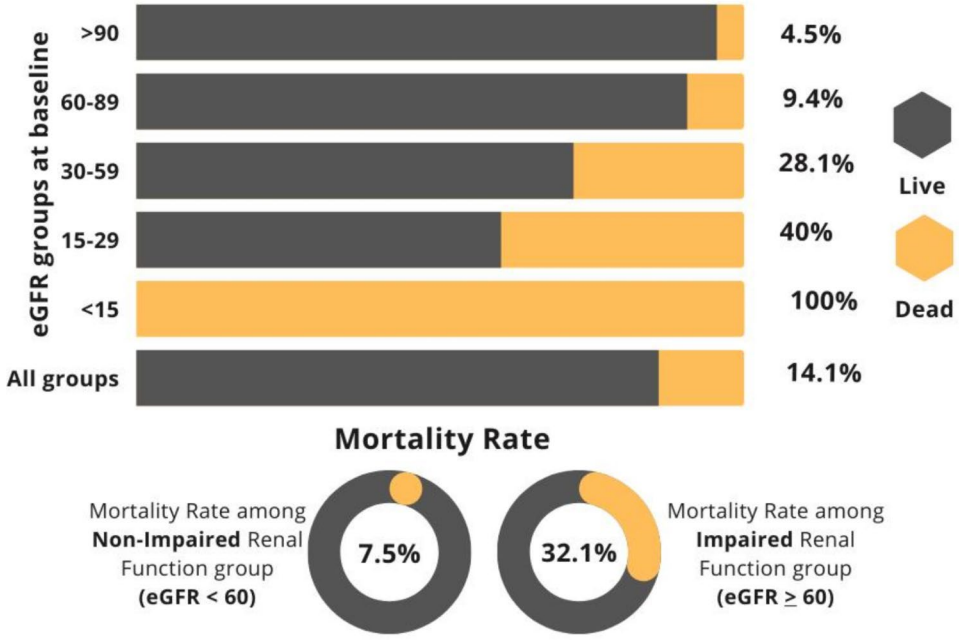

Fig. 3 Mortality rates at 3-year follow-up based on eGFR at baseline

Table 2 Relationship between background, clinical, laboratory predictors and eGFR decline

Variables	eGFR Decline		Multivariate Results		
	Yes *n* (%)	No *n* (%)	*P*-value	Adjusted *P*-value	Adjusted OR (95% CI)
Age at baseline*(Mean ± SD)*	63.1 ± 9.2	59.3 ± 10.5	0.002	0.296	1.02 (0.99–1.1)
Gender					
Male	76 (55.9%)	60 (44.1%)	< 0.001	< 0.001	5 (2.7–8.9)
Female*	32 (21.1%)	120 (78.9%)			
BMI at baseline *(Mean ± SD)*	32.3 ± 5.4	33.2 ± 6	0.184		
Smoker					
Yes	40 (44.9%)	49 (55.1%)	0.074	0.588	0.84 (0.46–1.6)
No*	65 (33.9%)	127 (66.1%)			
Hypertension					
Yes	93 (41.9%)	129 (58.1%)	0.001	0.033	2.4 (1.1–5.2)
No*	11 (19.0%)	47 (81.0%)			
HTN duration at baseline *(Mean ± SD)*	8.4 ± 7.5	8.9 ± 7.6	0.580		
DM duration at baseline *(Mean ± SD)*	12.5 ± 7.9	12.2 ± 8.3	0.810		
IRF at baseline (eGFR < 60)					
Yes	35 (50.0%)	35 (50.0%)	0.013	0.165	1.6 (0.83-3.0)
No*	73 (33.5%)	145 (66.5%)			
HbA1c at baseline *(Mean ± SD)*	8.6 ± 2.2	8.5 ± 2.02	0.667		
HDL cholesterol at baseline*(Mean ± SD)*	46.3 ± 11.7	47.7 ± 15.2	0.544		
LDL cholesterol at baseline*(Mean ± SD)*	86.1 ± 27.2	90.1 ± 30.8	0.409		

Reference group;IRF**: Impaired renal function, **OR**: Odds ratio, **CI**: Confidence interval*

Table 3 Relationship between background, clinical, laboratory predictors and all-cause mortality

Variables	All-cause mortality		Multivariate Results		
	Yes (*n* = 44)	No (*n* = 267)			
	Frequency	Frequency	*P*-value	Adjusted *P*-value	Adjusted OR (CI 95%)
Age at baseline*(Mean ± SD)*	64.4 ± 8.7	60.4 ± 10.3	0.014	0.831	1.01 (0.95–1.1)
Gender					
Male	29 (19.1%)	123 (80.9%)	0.015	0.701	0.79 (0.24–2.6)
Female*	15 (9.4%)	144 (90.6%)			
BMI at baseline *(Mean ± SD)*	32.3 ± 6	32.9 ± 5.7	0.522		
Smoker					
Yes	15 (15.6%)	81 (84.4%)	0.478	0.987	0.99 (0.3–3.2)
No*	26 (12.6%)	180 (87.4%)			
Hypertension					
Yes	37 (15.4%)	204 (84.6%)	0.149	0.740	0.75 (0.14–4.1)
No*	5 (8.2%)	56 (91.8%)			
HTN duration at baseline*(Mean ± SD)*	9.8 ± 8	8.7 ± 7.6	0.411		
DM duration at baseline *(Mean ± SD)*	13.6 ± 9.4	12.3 ± 8	0.331		
eGFR at baseline *(Mean ± SD)*	55.7 ± 26.4	76.6 ± 22.2	< 0.001		
IRF at baseline (eGFR < 60)					
Yes	27 (32.1%)	57 (67.9%)		0.002	5.5 (1.8–16.8)
No*	17 (7.5%)	210 (92.5%)	< 0.001		
GFR decline					
Yes	18 (16.7%)	90 (83.3%)	< 0.001	0.001	10.8 (2.8–41.6)
No*	3 (1.7%)	177 (98.3%)			
HbA1C at baseline *(Mean ± SD)*	8.1 ± 1.8	8.5 ± 2.1	0.215		
HDL cholesterol at baseline*(Mean ± SD)*	47.9 ± 12.2	47.2 ± 14.2	0.857		
LDL cholesterol at baseline*(Mean ± SD)*	92.7 ± 35.5	87.9 ± 29.3	0.535		

Reference group;IRF**: Impaired renal function, **OR**: Odds ratio, **CI**: Confidence interval*

baseline died compared to 7.5% of patients without IRF at baseline ($p < 0.001$). Furthermore, 16.7% of patients who experienced a decline in eGFR over three years died, while only 1.7% of those who did not experience a decline died ($p < 0.001$).

However, we found no statistically significant association between all-cause mortality and mean values of BMI, duration of both diabetes and hypertension, and factors such as smoking status, HbA1c, HDL, and LDL cholesterol levels. In multivariate regression analysis, we found that patients with IRF at baseline (aP-value = 0.002; aOR: 5.5; 95%CI: 1.8–16.8) and patients who developed eGFR decline (aP-value = 0.001; aOR: 10.8; 95%CI: 2.8–41.6) had significantly increased mortality rates.

Discussion

Diabetic nephropathy is characterized by a gradual eGFR decline, often without noticeable symptoms until the advanced stages of the disease. In this prospective cohort study, we aimed to assess the decline of eGFR, all-cause mortality, and the contributing risk factors among patients with diabetes. The study revealed that 37.5% of the patients experienced eGFR decline over the 3-year follow-up period, with an average annual decline rate of 4.2 ml/min/1.73 m2. This decline rate aligns with previously reported rates in different countries like Saudi Arabia (3.3 mL/min/1.73m2/year) [22], Brazil (4.7 ml/min/1.73 m2) [23] and Turkey (4.99 ml/min/1.73 m2) [24].

Several risk factors were identified as contributors to the decline in eGFR. Male patients had 5 times higher risk of experiencing eGFR decline, which aligns with previous research linking male gender to a decline in eGFR [25, 26]. Therefore, healthcare providers should closely monitor the renal function of diabetic male patients, potentially through more frequent assessments of eGFR and tailored treatment plans. These findings also highlight the importance of personalized, gender-specific approaches in diabetes care, recognizing that biological differences between males and females may significantly impact disease progression and outcomes.

Our study observed a significant association between hypertension and eGFR decline. Hypertensive patients were found to be 2.4 times more likely to experience a

decline in eGFR compared to patients without hypertension. This finding is consistent with previous studies [24, 27, 28]. Fluctuations in blood pressure directly impact kidney function, and high blood pressure deteriorates CKD, leading to an increased incidence of ESRD and a heightened risk of cardiovascular diseases [29, 30]. Additionally, dietary habits in Palestine, which combine traditional plant-based foods with an increasing intake of Western-style processed items, may contribute to a decline in kidney function [31]. The increased intake of high-salt, sugary, and fried foods -with an average salt intake of 7 g per day in Palestine [32] - may exacerbate hypertension and its associated complications [33]. Recognizing the connection between hypertension and a decline in eGFR highlights the importance of closely managing blood pressure in patients with diabetes to mitigate kidney damage. Early identification and treatment of hypertension have the potential to slow down the rate of eGFR decline, thereby delaying ESRD and the need for dialysis or kidney transplantation.

Early in the course of diabetic nephropathy, there is a hyperfiltration phase that leads to an increase in eGFR. The dilation of the afferent glomerular arteriole, caused by hormones and vasoactive substances that are elevated in patients with diabetes, such as insulin-like growth factor 1, atrial natriuretic peptide, sex hormones, intracellular sorbitol, and early glycation products, plays an important role in hyperfiltration [34]. This can explain the phenomenon in Fig. 2, as patients in the eGFR ≥ 60 group exhibited a higher mean eGFR at 3-year follow-up than the baseline.

The study also found a correlation between IRF at baseline and eGFR decline. This can be explained by the fact that nephron loss occurs early in diabetic nephropathy, with the remaining nephrons undergoing hypertrophy to sustain the GFR. However, there is a point where this compensatory mechanism reaches its limit, resulting in a rapid decline in eGFR as more nephrons are lost [35].

Over the 3-year follow-up period, we observed that 14.1% of our patients died, resulting in an all-cause mortality rate of 51.3 deaths per 1000 person-years. This is comparable to a study in the United States of America, which reported an all-cause mortality rate of 50.6 per 1000 person-years [36]. Other studies conducted in Iran, Taiwan, and Korea also reported rates of 38.2, 29.6, and 24.5 per 1000 person-years, respectively [37–39].

Various factors influence the all-cause mortality in patients with diabetes. Our investigations revealed that as eGFR decreases, mortality rates increase (Fig. 3). We observed 27% of our patients had IRF (eGFR < 60) at baseline. These individuals faced a significantly higher risk of all-cause mortality which was 5.5 times higher compared to those without impairment. Moreover, patients who exhibited a decline in eGFR had a 10.8 times higher risk of all-cause mortality than those with no eGFR decline, as indicated in Table 3. This finding is consistent with other studies that have demonstrated a substantial increase in all-cause mortality in patients with eGFR decline [22, 40].

These noteworthy results highlight the necessity of more vigilant surveillance of patients in advanced stages of diabetic nephropathy, with a specific emphasis on identifying and addressing the factors that contribute to mortality. They also highlight the need for early interventions that preserve kidney function to improve the prognosis for diabetic individuals.

.While this study provides valuable insights, there are a few limitations to consider. Some patients could not attend their scheduled appointments at PHC centers during the follow-up period, likely due to the impact of the COVID-19 pandemic. This led to incomplete data in their records, with 75 patients excluded due to loss of follow-up, resulting in a relatively small cohort. Additionally, limited resources in primary care settings resulted in insufficient data on albuminuria. Although comorbidity factors were addressed, the study did not explore the effect of targeted interventions on GFR progression. This could further enhance our understanding of the factors influencing kidney function decline.

Conclusion

The study demonstrates that the eGFR declined at a rate of 4.2 ml/min/1.73 m2 per year among T2DM patients. This decline was significantly associated with male gender, hypertension, and IRF. Moreover, the all-cause mortality rate was 51.3 deaths per 1000 person-years. Individuals with IRF and GFR decline were found to have a higher risk of all-cause mortality. This study highlights the importance of early detection of CKD in patients with diabetes, prompting more comprehensive management of risk factors related to GFR decline and mortality. Furthermore, it underscores the need for future research in this patient population to investigate the impact of different medications, such as anti-diabetic and antihypertensive medications, on the rate of GFR decline and mortality.

Acknowledgements

We would like to extend our appreciation to the Ministry of Health and An-Najah National University for their support and assistance in facilitating access to primary healthcare centers. Additionally, we acknowledge the support provided by primary healthcare physicians at diabetic clinics. Lastly, we would like to express our sincere gratitude to the participants who took part in the research.

Author contributions

ZN and ZH contributed to the study's concept and supervised its implementation. ZN, ZH, and MH designed the study and its methods, as well as critically reviewed and revised the manuscript. Under ZN supervision, MJ, AS, and KN collected data, performed data analysis, and wrote the first draught of the manuscript. The final version of the manuscript was revised and approved by all authors.

Funding
No funding was received for this study from any source.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
All procedures were carried out in compliance with relevant national guidelines and regulations, laws, and the Declaration of Helsinki. The study and its protocols received approval from the Institutional Review Board committee of An-Najah National University [Reference #: Med. Sep. 2021/8]. No identifying information was collected. The need for informed consent was deemed unnecessary for this study as we relied on patients' electronic medical records and patient files to collect relevant data. However, patients who agreed to participate in the baseline study signed an informed consent document, assuring them of their privacy and confidentiality.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 16 December 2023 / Accepted: 6 January 2025
Published online: 10 February 2025

References

1. Molitch ME, DeFronzo RA, Franz MJ, Keane WF, Mogensen CE, Parving HH, et al. Nephropathy in diabetes. Diabetes Care. 2004;27(Suppl 1):S79–83.
2. Qaddumi JAS, Nazzal Z, Yacoup ARS, Mansour M. Quality of death notification forms in North West Bank/Palestine: a descriptive study. BMC Res Notes. 2017;10(1).
3. Association AD. Standards of Medical Care in Diabetes—2017 Abridged for Primary Care Providers. Clin Diabetes [Internet]. 2017;35(1):5–26. Available from: https://doi.org/10.2337/cd16-0067
4. Journal O, Society I. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. 2013;3(1).
5. Schaeffner ES, Ebert N, Kuhlmann MK, Martus P, Mielke N, Schneider A, et al. Age and the course of GFR in persons aged 70 and above. Clin J Am Soc Nephrol. 2022;17(8):1119–28.
6. Tziomalos K, Athyros VG. Diabetic nephropathy: New risk factors and improvements in diagnosis. Rev Diabet Stud. 2015;12(1):110–8.
7. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR. Risk factors for renal dysfunction in type 2 diabetes: U.K. prospective diabetes study 74. Diabetes. 2006;55(6):1832–9.
8. Meeme A, Kasozi H. Effect of glycaemic control on glomerular filtration rate in diabetes mellitus patients. Afr Health Sci. 2009;9(Suppl 1):23–6.
9. Afkarian M, Sachs MC, Kestenbaum B, Hirsch IB, Tuttle KR, Himmelfarb J et al. Kidney Disease and Increased Mortality Risk in Type 2 Diabetes. J Am Soc Nephrol. 2013;24(2):302 LP – 308.
10. Thomas MC, Brownlee M, Susztak K, Sharma K, Jandeleit-Dahm KAM, Zoungas S, et al. Diabetic kidney disease. Nat Rev Dis Prim. 2015;1:15018.
11. BLONDE L, VASSALOTTI JA, PILON D, WYNANT W, ZHDANAVA M, LEFEBVRE P, et al. 14-OR: the cost of chronic kidney Disease Progression in type 2 diabetes patients. Diabetes. 2019;68(Supplement1):14–OR.
12. Golestaneh L, Alvarez PJ, Reaven NL, Funk SE, McGaughey KJ, Romero A, et al. All-cause costs increase exponentially with increased chronic kidney disease stage. Am J Manag Care. 2017;23(10 Suppl):S163–72.
13. Abu-Rmeileh NMEE, Husseini A, Capewell S, Flaherty MO, O'Flaherty M. Preventing type 2 diabetes among palestinians: comparing five future policy scenarios. BMJ Open. 2013;3(12):1–6.
14. Ahmed N, Khderat AH, Sarsour A, Taher A, Hammoudi A, Hamdan Z, et al. The vulnerability of maintenance dialysis patients with COVID-19: mortality and risk factors from a developing country. Ann Med. 2022;54(1):1511–9.
15. Jebril M, Liu X, Shi Z, Mazidi M, Altaher A, Wang Y. Prevalence of type 2 diabetes and its association with added sugar intake in citizens and refugees aged 40 or older in the gaza strip, palestine. Int J Environ Res Public Health. 2020;17(22):1–15.
16. Ministry of Health 2019. Ministry of Health. (2019). Annual Report for Ministry of Health in Palestine. Retrieved from www.moh.ps. 2019.
17. Abdel-Hafez Y, Siaj H, Janajri M, Abu-Baker Y, Nazzal Z, Hamdan Z, et al. Tolerability and epidemiology of nephrotoxicity associated with conventional amphotericin B therapy: a retrospective study in tertiary care centers in Palestine. BMC Nephrol. 2022;23(1):132.
18. Qaddumi JAS, Nazzal Z, Yacoub A, Mansour M. Physicians' knowledge and practice on death certification in the North West Bank, Palestine: across sectional study. {BMC} Heal Serv Res [Internet]. 2018;18(1). Available from: https://doi.org/10.1186%2Fs12913-017-2814-y
19. Nazzal Z, Hamdan Z, Masri D, Abu-Kaf O, Hamad M. Prevalence and risk factors of chronic kidney disease among Palestinian type 2 diabetic patients: a cross-sectional study. BMC Nephrol [Internet]. 2020 Dec 1 [cited 2024 Mar 9];21(1). Available from: https://pubmed.ncbi.nlm.nih.gov/33198669/
20. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604–12.
21. Stevens LA, Li S, Kurella Tamura M, Chen SC, Vassalotti JA, Norris KC, et al. Comparison of the CKD Epidemiology Collaboration (CKD-EPI) and modification of Diet in Renal Disease (MDRD) study equations: risk factors for and complications of CKD and mortality in the kidney early evaluation program (KEEP). Am J Kidney Dis off J Natl Kidney Found. 2011;57(3 Suppl 2):S9–16.
22. Alwakeel JS, Isnani AC, Alsuwaida A, Alharbi A, Shaikh SA, Almohaya S, et al. Factors affecting the progression of diabetic nephropathy and its complications: a single-center experience in Saudi Arabia. Ann Saudi Med. 2011;31(3):236–42.
23. Trevisan R, Vedovato M, Mazzon C, Coracina A, Iori E, Tiengo A et al. Concomitance of Diabetic Retinopathy and Proteinuria accelerates the rate of decline of kidney function in type 2 Diabetic patients.
24. Unsal A, Koc Y, Basturk T, Akgun AO, Sakaci T, Ahbap E. Risk factors for progression of renal disease in patient with diabetic nephropathy. Eur Rev Med Pharmacol Sci. 2012;16(7):878–83.
25. Eriksen BO, Ingebretsen OC. The progression of chronic kidney disease: a 10-year population-based study of the effects of gender and age. Kidney Int. 2006;69(2):375–82.
26. Swartling O, Rydell H, Stendahl M, Segelmark M, Trolle Lagerros Y, Evans M. CKD Progression and Mortality among men and women: a Nationwide Study in Sweden. Am J Kidney Dis off J Natl Kidney Found. 2021;78(2):190–e1991.
27. Bakris GL, Weir MR, Shanifar S, Zhang Z, Douglas J, van Dijk DJ, et al. Effects of blood pressure level on progression of diabetic nephropathy: results from the RENAAL study. Arch Intern Med. 2003;163(13):1555–65.
28. Lee H, Kwon SH, Jeon JS, Noh H, Han DC, Kim H. Association between blood pressure and the risk of chronic kidney disease in treatment-naïve hypertensive patients. Kidney Res Clin Pract. 2022;41(1):31–42.
29. Anderson AH, Yang W, Townsend RR, Pan Q, Chertow GM, Kusek JW, et al. Time-updated systolic blood pressure and the progression of chronic kidney disease: a cohort study. Ann Intern Med. 2015;162(4):258–65.
30. Hanratty R, Chonchol M, Havranek EP, Powers JD, Dickinson LM, Ho PM, et al. Relationship between blood pressure and incident chronic kidney disease in hypertensive patients. Clin J Am Soc Nephrol. 2011;6(11):2605–11.
31. Mikki N, Abdul-Rahim HF, Shi Z, Holmboe-Ottesen G. Dietary habits of Palestinian adolescents and associated sociodemographic characteristics in Ramallah, Nablus and Hebron governorates. Public Health Nutr. 2010;13(9):1419–29.
32. Awwad R, Qasrawi R, Alwafa RA, Kharaz L, Badrasawi M. Development and validation of food frequency questionnaire screener software for sodium intake among Palestinian population. BMC Nutr. 2024;10(1).
33. Halbach SM. Hypertension in chronic kidney disease. Pediatr Hypertens Fifth Ed. 2023;477–98.
34. Yang Y, Xu G. Update on Pathogenesis of Glomerular Hyperfiltration in Early Diabetic kidney disease. Front Endocrinol (Lausanne). 2022;13(May):1–11.
35. Schnaper HW. Remnant nephron physiology and the progression of chronic kidney disease. Pediatr Nephrol. 2014;29(2):193–202.
36. Raghavan S, Vassy JL, Ho YL, Song RJ, Gagnon DR, Cho K et al. Diabetes mellitus–related all-cause and cardiovascular mortality in a national cohort of adults. J Am Heart Assoc. 2019;8(4).
37. Salehidoost R, Mansouri A, Amini M, Aminorroaya Yamini S, Aminorroaya A. Diabetes and all-cause mortality, a 18-year follow-up study. Sci Rep. 2020;10(1):3183.

38. Wang JS, Wu YL, Ou HY, Yang YS, Hsu CC, Hwu CM. Trends in all-cause mortality and major causes of death between 2007 and 2018 among patients with diabetes in Taiwan. Front Endocrinol (Lausanne). 2022;13(August):1–7.
39. Kang YM, Kim YJ, Park JY, Lee WJ, Jung CH. Mortality and causes of death in a national sample of type 2 diabetic patients in Korea from 2002 to 2013. Cardiovasc Diabetol. 2016;15(1):1–10.
40. González-Pérez A, Saez M, Vizcaya D, Lind M, Garcia Rodriguez L. Incidence and risk factors for mortality and end-stage renal disease in people with type 2 diabetes and diabetic kidney disease: a population-based cohort study in the UK. BMJ open Diabetes Res care. 2021;9(1).

Publisher's note