Alqalam Journal of Medical and Applied Sciences. 2026;9(5):1140-1146
https://doi.org/10.54361/ajmas.269503

Original article

Impact of Low-Protein Dietary Intervention on Albuminuria in Diabetic Nephropathy: A Clinical Trial

Hajer Mohammed*[1], Hana Alshaky[2], Seham Elgallal[2], Hameida Elfarssi[1]

[1]*Department of Nutrition, Faculty of Public Health, University of Benghazi, Benghazi, Libya*
[2]*Nephrology Center, Benghazi, Libya*
Corresponding Email. hajer.mohammed@uob.edu.ly

Abstract
Diabetic Nephropathy (DN) represents one of the leading causes of end-stage renal disease (ESRD) and imposes a substantial clinical and economic burden. Microalbuminuria, recognized as an early marker of DN, is associated with heightened cardiovascular risk. While renin-angiotensin system inhibition and glycemic control are the strategies now, the role of a low-protein diet (LPD) in modulating DN and associated metabolic derangements remains under debate. This study assessed the impact of LPD on kidney function and metabolic indicators in type II diabetic patients and recently diagnosed with albuminuria. An 11-month prospective, randomized, controlled study that enrolled 80 patients suffering from type II diabetes and recently diagnosed with albuminuria. Participants were randomized into three groups: ACE-I/ARB, LPD (0.6 g/kg/day), and LPD + ACE-I/ARB groups. In this study, we evaluated renal function (GFR, UAER), glycemic controls (FBS, HbA1c), and metabolic indicators (BMI, blood pressure, lipid profile) at the start and conclusion of the study. All study groups showed a significant reduction in albuminuria ($p< 0.05$) in the within-group comparison. Meanwhile, group comparison showed no statistical variation in UAER. Furthermore, GFR showed improvement in the LPD group, but it wasn't statistically significant. Moreover, the LPD group showed significant reductions in FBS, HbA1C, LDL, T.G, systolic blood pressure, and BMI (all $p < 0.05$); these effects weren't observed in other groups. LPD in type II diabetes effectively reduces albuminuria in comparison to ACE-I/ARB therapy. Moreover, LPD shows significant benefits regarding glycemic control, lipid profile, and body weight. These results suggest that the therapeutic potential of LPD to manage diabetic nephropathy and its metabolic complications highlights the critical role of dietary management.
Keywords. Albuminuria, Diabetic Nephropathy, Low Protein Diet, Kidney Function, Type II Diabetes.

Introduction

DN represents a significant microvascular complication of DM, and a key cause of ESRD worldwide [1,2]. With a prevalence affecting roughly 30% of type 1 and 40% in type II diabetes, the pathogenesis of DN is frequently preceded by signs such as glomerular hyperfiltration and microalbuminuria [3,4]. Microalbuminuria is a sign of renal impairment as well as a strong biomarker of systemic microvascular damage, encompassing retinopathy, neuropathy, and ischemic heart disease, and is correlated with a marked increase in all-cause mortality among diabetic patients [5,6,7]. The current practices to attenuate the progression of DN include stringent glycemic control and the blockade of the renin-angiotensin system [8,9].

The physiological impact of dietary protein on renal function is well-documented; elevated protein consumption can induce a rise in glomerular filtration rate (GFR), similar to the renal adoptive mechanisms observed post-nephrectomy [10]. This insight has spurred significant interest in employing low-protein diets (LPDs) as a therapeutic approach to decelerate the advancement of diabetic renal disease, promoting their recommendation in certain clinical guidelines for individuals with established chronic kidney disease [11,12].

Despite numerous investigations on the effect of LPD on renal outcomes in diabetic populations, the reported findings remain inconsistent. variant results have been reported between studies of varying duration, including both short- and long-term interventions, in addition to findings from meta-analyses [11,13-18]. This inconsistency highlights a substantial gap concerning the precise and holistic benefits of LPD, especially when evaluated against or in combination with conventional pharmacotherapy, preserving kidney function and modulating metabolic parameters in individuals with incipient albuminuria. Resolving this uncertainty is vital for refining treatment paradigms for DN. Consequently, this study was designed to assess the efficacy of an LPD on kidney function, glycemic control, and lipid metabolism in individuals suffering from type II diabetes recently diagnosed with albuminuria, comparing its effects to standard ACE-I/ ARB therapy and a combined therapeutic approach.

Methodology

Research Design

The research was a prospective, randomized, controlled trial conducted over an 11-month duration, from July 1, 2024, to June 30, 2025, at the Nephrology Center. Patients were recruited after referral from a diabetes center where they received diabetes care, and received care from the same physician and dietitian

Received: *28-02-2026* - ***Accepted***: *26-04-2026* - ***Published***: *02-05-2026*

throughout the study. The ethics committee of the hospital accepted the research protocol (no.777), and all subjects provided written permission prior to enrollment.

Sample size

Based on the primary outcome change [19], a total of 66 participants, about 22 per group, were required to detect a difference within the groups with 80% power at α= 0.05. And to account for dropout, 90 patients were recruited.

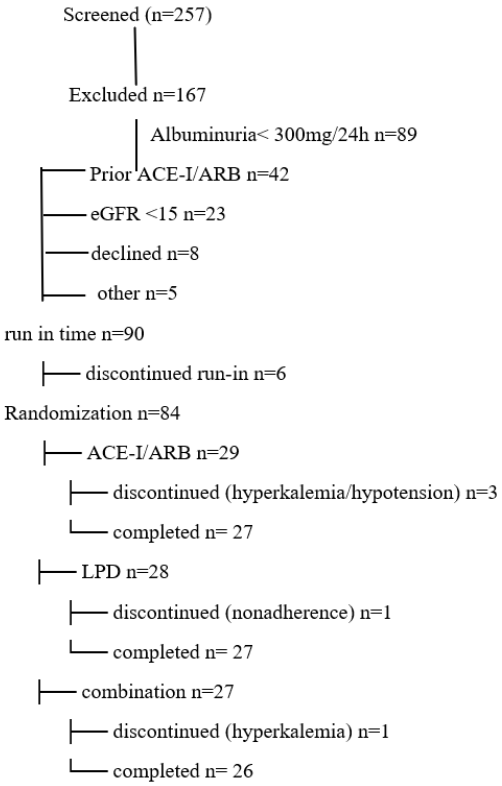

Figure 1. Visual Consort Flow Structure

Participants

Initially, a total of 90 patients were recruited. During the run-in period, 6 participants were excluded, and the remaining 84 participants were randomized into 3 groups. During the intervention, 4 discontinued. Finally, 80 individuals (48 males, 32 females), with an age ranged 30 to 70 years, with type II diabetes (diagnosed per WHO standard) completed the study. Inclusion criteria included: (1) recent diagnosis of diabetic nephropathy, and (2) albuminuria (microalbuminuria < 300 and macroalbuminuria ≥300 mg/24 h) in two out of three sterile urine samples, and no clinical or test indication of other kidney or urinary tract disorders. Exclusion criteria were: (1) type 1 diabetes, (2) malignant hypertension or (3) prior use of angiotensin II receptor blockers (ARBs) or ACE inhibitors (ACE-I), within 3 months of enrollment (4) a history of heart diseases, liver disease, cancer, (5) morbid obesity (BMI _ 35 kg/m^2), (6) frequent episodes of urinary tract infection and ESRD (GFR < 15 mL/min/ 1.73m^2 using CKD-EPI 2021). Blood pressure of ≥140/90 mmHg, or the use of non-ACE/ARB antihypertensive medications, was considered hypertension.

Randomization and Intervention

After a three-month run-in phase, participants were randomized in a 1:1:1 ratio into three treatment groups, with stratification based on baseline urinary albumin excretion rate (UAER; 300–1000 mg/24 hrs versus >1000 mg/24 hrs) to ensure balanced distribution of disease severity across the groups. During the run-in, all patients received standardized guidance aimed at achieving optimal metabolic control through dietary modifications and the use of insulin or oral hypoglycemic agents. The first intervention group received standard care with ACE inhibitors or angiotensin receptor blockers, specifically enalapril administered at 10 mg twice daily and titrated to 20 mg twice daily, or losartan initiated at 50 mg/day and titrated to 100 mg/day. The second group was assigned to a low-protein diet (LPD), with counseling to achieve a daily protein intake of 0.6 g/kg. The dietary plan emphasized high biological value protein sources, with more than half derived from eggs, fish, poultry, and dairy products. To support adherence, participants were provided with a seven-day menu plan and cooking instructions. The third group received a combination of both interventions, integrating pharmacological therapy with dietary restriction. Given the nature of the dietary intervention, blinding of investigators and participants was not feasible. This design allowed for the

Received*: 28-02-2026 -* ***Accepted****: 26-04-2026 -* ***Published****: 02-05-2026*

systematic evaluation of pharmacological, nutritional, and combined strategies in the management of chronic kidney disease progression.

Monitoring of adherence

Protein intake adherence was assessed by (1) a three-day food record, and (2) 24-hour urea and protein intake calculated by [24hUUN(g) + 0.031 g/kg x weight] [20]. Non-adherence (patients > 20% of recommended protein intake) received intensified counseling, and pill counts and prescription refill were used to assess medication adherence.

Clinical and Laboratory Measurements

Clinical and laboratory evaluations were conducted at both baseline and study conclusion to ensure a comprehensive assessment of patient status. Anthropometric measurements included height, weight, and body mass index, calculated as kilograms per square meter. Blood pressure was measured after five minutes of rest using a mercury sphygmomanometer, with three readings taken and the mean of the final two used for analysis. Kidney function was evaluated through estimated glomerular filtration rate (eGFR), calculated using the Cockcroft–Gault formula, and urinary albumin excretion rate (UAER), which was determined by nephelometry from sterile 24-hour urine samples (Beckman Instrument, Germany, order no. 441450). Glycemic status was assessed by fasting blood glucose and glycated hemoglobin (HbA1c), with HbA1c quantified using ion-exchange high-performance liquid chromatography (Merck, Darmstadt, Germany). Lipid profile analysis was performed on fasting blood samples using automated methods (Roche/Hitachi 917; CAN 690, USA), measuring total cholesterol, high-density lipoprotein cholesterol, and triglycerides, while low-density lipoprotein cholesterol was calculated using the Friedewald equation [21]. This standardized evaluation protocol provided a robust dataset for monitoring metabolic, renal, and cardiovascular parameters throughout the study.

Monitoring of safety

Predefined criteria for adverse effects were reviewed throughout study time (1) increase in s.cr by 50% from baseline and persisted > 4 weeks; (2) hyperkalemia; (3) hypotension, SBP< 90mmHg. Any of these adverse effects was reported to the ethics committee within 48 hours.

Data analysis

Results are presented as means ± SD. Initial assessment of the difference between the 3 groups was conducted using one-way *ANOVA*. Upon finding significant ANOVA results, further analysis involved: unpaired t-tests for comparisons between different groups (Inter-group). A p-value of less than 0.05 was considered of significance statistically significant. Data analysis was conducted using SPSS (V20.0).

Results

Patient Characteristics

Initially, this study enrolled 84 patients, with 4 discontinued in the intervention period. The remaining 80 patients were randomly allocated into 3 groups: ACE/ARB (n=27), LPD (n=27), and Combination (n=26). Key demographic and clinical characteristics at the start are detailed in (Table 1). Across the study group, the average age varied between 51 and 59.2 years. Males constituted a higher proportion in all groups (51.8% to 69.2%). Hypertension was prevalent, affecting 50.0% to 74.1% of participants. Smoking prevalence varied, with the Combination group having the lowest percentage (30.7%). Microalbuminuria (30-299 mg/24hrs) and macroalbuminuria (>300 mg/24hrs) were distributed in the groups as shown in (Table 1).

Table 1. Demographic and Clinical Profile of Participants (n=80)

Variable	ACEI /ARB n=27(%)	LPD n=27(%)	Combination n=26 (%)
Age (mean, SD)	59.2 ± 25.3	54.6 ± 15.6	51± 12.8
Gender (Male, %)	14 (51.8)	16(59.2)	18(69.2)
HTN (n, %)	20 (74.1)	14 (51.9)	13 (50.0)
Treatment (n, %)			
Oral hypoglycemic agent	9 (33.3)	9 (33.3)	7 (26.9)
Insulin	9 (33.3)	9 (33.3)	6 (23.1)
Both	9 (33.3)	9 (33.3)	13 (50.0)
Smoking (n, %)	14 (51.9)	14 (51.9)	8 (30.7)
Albumin in urine (n, %)			
Microalbuminuria (30-299mg/24hrs)	14 (51.9)	14 (51.9)	6 (23.1)
Macroalbuminuria (> 300mg/24hrs)	13 (48.5)	13 (48.5)	20 (76.9)

Received*: 28-02-2026 -* ***Accepted****: 26-04-2026 -* ***Published****: 02-05-2026*

Interventions Effect on Renal Function

All three intervention groups demonstrated a significant intra-group reduction in UAER from baseline (p value < 0.05). specifically, UAER decrease from 441.6 ± 387mg to 291.4 ± 343.8 mg in the ACE/ARB group, from 700.7 ± 228.2 mg to 355.6 + 449.5 mg in the LPD group, and from 819.3 + 703.3 mg to 517.8 +715.0 mg in Combination group. However, inter-group comparisons revealed no significant differences in UAER, which showed no statistical variation among the three groups. GFR did not show a significant change in any of the groups (Figures 2 and 3).

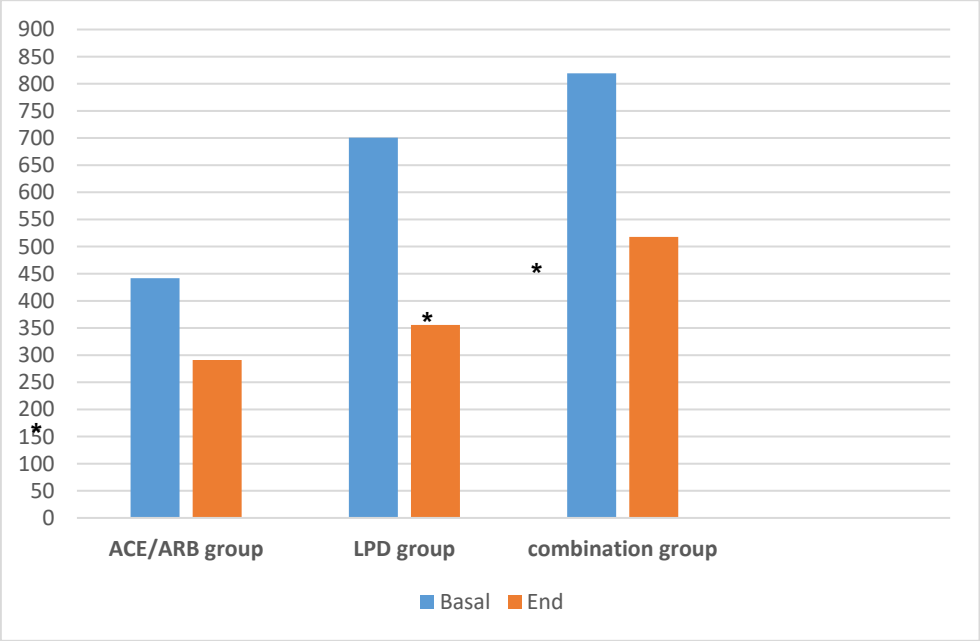

Figure 2. Impact of Interventions on UAER (mg/24 hours) (n=80)
(*) statistically significant (p value <0.05) in intra-group comparison

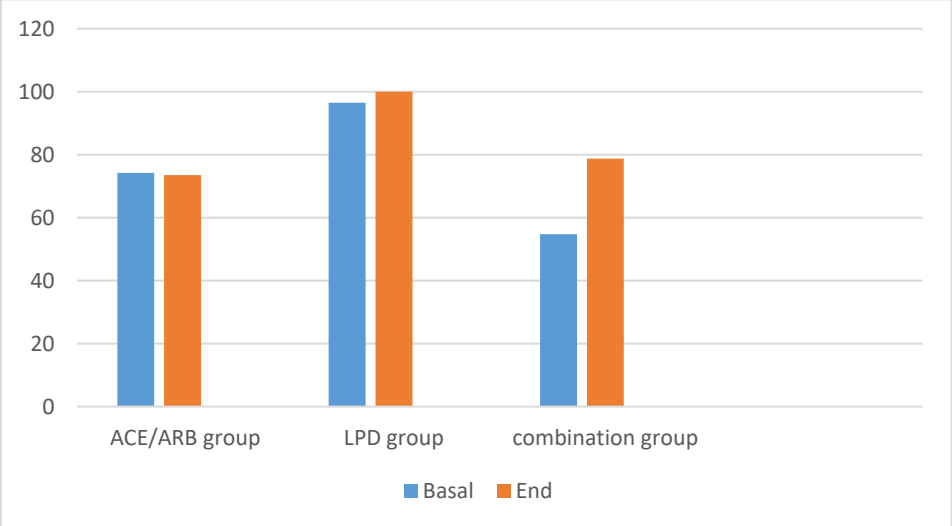

Figure 3. Impact of Interventions on GFR (mL/min) (n=80)

Interventions Effect on Metabolic Control

Significant reductions in intra-group comparison in FBS and HbA1c were observed in both the LPD and Combination groups. In the LPD group, FBS decreased from 186.70 + 22.60 mg/dl to 162.2 + 31.40 mg/dl, and HbA1c declined from 9.1 ± 1.3% to 8.0 ± 0.6%. in the Combination group, FBS decreased from 205.3 ± 99.2 mg/dl to 144.53 ± 40.52 mg/dl, and HbA1c decreased from 8.4 ± 1.8% to 7.8 ± 1.5%. The LPD group also showed a significant decline in intra-group and inter-group comparison in systolic blood pressure, decreased from 123.7 ± 12.5 mmHg to 99.75 ± 3.30 mmHg (Table 3). Moreover, BMI showed a significant reduction in the LPD group.

Interventions Effect on Lipid Profile

Received*: 28-02-2026 -* ***Accepted****: 26-04-2026 -* ***Published****: 02-05-2026*

All groups showed a significant reduction in intra-group comparison in total cholesterol level ($p < 0.05$). TC decreased from 155.4 ± 32.6 mg/dl to 152.6 ± 24 mg/dl in the ACE/ARB group, from 149.7 ± 33.4 mg/dl to 141.7 ± 42 mg/dl in the LPD group, and from 155 ± 66 mg/dl to 150 ± 47.9 mg/dl in the Combination group. No significant inter-group differences were noticed for TC. Furthermore, the LPD group demonstrated a significant reduction in LDL (91.2 ± 5.31 mg/dl to 88.2 ± 4.0 mg/dl) and T.G (126 ± 55.7 mg/dl to 111 ± 51.6 mg/dl) (Table 4).

Table 2. Interventions' Effect on Metabolic Control and Lipid Profile

Parameters	Groups	Basal (mean +SD	End (mean +SD)	P-value (intra-group)
FBS (mg/dl)	LPD	186.7 + 22.6	162.2 + 31.4	< 0.05
	Combination	205.3 + 99.2	144.5 +40.5	< 0.05
HbA1c (%)	LPD	9.1 +1.3	8.0 +0.6	< 0.05
	Combination	8.4 + 1.8	7.8 + 1.5	< 0.05
Systolic BP	LPD	123.7 +12.5	99.75 + 3.3.	< 0.05
TC (mg/dl)	ACE/ARB	155.4 + 32.6	152.6 + 24.0	< 0.05
	LPD	149.7 + 33.4	141.7 + 42.0	< 0.05
	Combination	155.0 + 66.0	150.0 + 47.9	< 0.05
LDL (mg/dl)	LPD	91.2+ 5.31	88.2 + 4.0	< 0.05
Triglycerides	LPD	126.0 + 55.7	111.0 + 51.6	< 0.05

Discussion

This study evaluates the impact of low protein on kidney function, alongside metabolic markers in type II diabetes patients with new onset albuminuria, comparing against ACE-I/ARB treatment and combined intervention. Key results indicate that LPD significantly lowered UAER to a degree similar to pharmaceutical intervention. Moreover, the LPD group showed marked enhancements in glycemic control, lipid metabolism, and reduction in body weight, highlighting its potential as a comprehensive treatment approach for DN and its related metabolic disorders.

The significant decrease in UAER across all treatment groups, notably the LPD group, is consistent with existing literature supporting the renal benefits of both dietary protein moderation and pharmacological RAS suppression [22,23]. The finding that LPD reduction of UAER is comparable to ACE-I/ARB therapy highlights dietary adjustment as a viable non-pharmaceutical strategy for mitigating this important indicator of renal impairment. The renoprotective mechanisms of LPD are multifactorial. High protein consumption stimulates glucagon secretion, resulting in afferent arteriolar vasodilation and elevated intra-glomerular pressure, which can worsen albuminuria [24]. LPD may counter these adverse hemodynamic effects. Moreover, excessive protein can increase insulin-like growth factor-1, also known as a renal vasodilator, while LPD appears to suppress the internal renin-angiotensin system, thereby supporting kidney function [25]. Although UAER improvements were clear, the absence of a statistically significant alteration in GFR within the LPD group despite a positive trend from baseline. This outcome agrees with systematic reviews and prospective investigations [26,27], but conflicts with other studies of notable GFR enhancement during LPD [28]. Discrepancies in GFR results across studies may arise from variables such as participant baseline renal function, LPD may preserve GFR more effectively in individuals with initially reduced function, while lowering it in those with higher baseline GFR [22], inaccuracies in creatinine-based GFR estimation [29], or methodological differences [15]. Future studies using more accurate GFR assessment methods and subgroup analyses by initial kidney function may help clarify these inconsistencies.

A significant strength of this study lies in metabolic improvements such as BG, HbA1C, systolic blood pressure, LDL, TC, TG, and BMI within the LPD group. These benefits were not consistently evident in the ACE-I/ARB or in combination groups, indicating a distinct effect of dietary protein restriction. Our results are in agreement with other works associating LPD with better glycemic management, blood pressure control, and lipid metabolism in the diabetic population [28,30]. The physiological basis for these metabolic effects is likely diverse. Substituting protein with carbohydrate and fiber-rich foods, common in LPD, may help in glycemic control [31,32]. Moreover, weight loss, as noted in the LPD group, is a recognized modulator of metabolic health in type II diabetes with obesity [33]. Reduction in LDL and T.G levels, in the absence of lipid-lowering medication, implies that inherent aspects of LPD, such as lower fat and cholesterol consumption, contribute to a positive effect [34]. These outcomes position LPD not only as a renoprotective diet, but also as a systemic intervention with multi-organ benefits [35].

Conclusion

This research highlights the value of moderate protein restriction (0.6g/kg/day) as a supportive therapeutic approach in reducing albuminuria in type II diabetes with conventional drug therapies. The added metabolic

Received*: 28-02-2026 -* ***Accepted****: 26-04-2026 -* ***Published****: 02-05-2026*

gains in glucose, lipids, and weight management suggest LPD should be incorporated into integrated care strategies for diabetic nephropathy, especially considering the established interplay between albuminuria and cardiovascular risk factors like hyperglycemia, hypertension, dyslipidemia, and obesity. Subsequent studies should assess long-term adherence to LPD and determine protein consumption thresholds for different nephropathy stages. Further, larger trials with extended follow-up are necessary to determine the lasting influence of LPD on definitive endpoints such as ESRD and cardiovascular morbidity. Elucidating the molecular pathways through which LPD imparts metabolic benefits could also inform future therapeutic strategies. Limitations. Several limitations should be mentioned. The sample size (n=80), though adequate for detecting within-group changes, may be underpowered for more nuanced between-group comparisons or broader generalization. The reliance on estimated GFR derived from S.Cr c, while practical, is imperfect and might not reflect small changes in renal function. Precisely measuring long-term dietary adherence is inherently difficult. Lastly, the 11-month duration, though considerable, may be insufficient for a comprehensive evaluation of the long-term renal effect of LPD.

Conflicts of interest
No conflicts of interest were declared by the authors.

Funding
This study received no external funding.

Competing interests
The authors declare no competing interests

References
1 Crael LP, Bornett D, Levine R. The history of diabetes. In: Kahn ER, Weir GC, editors. Joslin's diabetes mellitus. New Delhi: B.I. Waverly; 1994.
2 Alicic RZ, Tuttle KR. Management of the diabetic patient with advanced chronic kidney disease. Semin Dial. 2010;23(2):140-7. doi:10.1111/j.1525-139X.2010.00700.x
3 Ritz E, Orth SR. Nephropathy in patients with type 2 diabetes mellitus. N Engl J Med. 1999;341(15):1127-33. doi:10.1056/NEJM199910073411506
4 Foley RN, Collins AJ. End-stage renal disease in the United States: an update from the United States Renal Data System. J Am Soc Nephrol. 2007;18(10):2644-8.
5 Sasso FC, De Nicola L, Carbonara O, et al. Cardiovascular risk factors and disease management in type 2 diabetic patients with diabetic nephropathy. Diabetes Care. 2006;29(3):498-503. doi:10.2337/diacare.29.03.06.dc05-1776
6 Bhavya N, Kumar VA. Study of association between microalbuminuria and microvascular complications in Type II diabetes mellitus patients in RajaRajeswari Medical college and hospital, Karnataka. Jf Medi Scis. 2017;3(1):6-10. doi:10.5005/jp-journals-10045-0046
7 Valmadrid CT, Klein R, Moss SE, Klein BE. The risk of cardiovascular disease mortality associated with microalbuminuria and gross proteinuria in persons with older-onset diabetes mellitus. Arch Intern Med. 2000;160(8):1093-100. doi:10.1001/archinte.160.8.1093
8 Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group. N Engl J Med. 1993;329(20):1456-62. doi:10.1056/NEJM199311113292004
9 Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329(14):977-86. doi:10.1056/NEJM199309303291401
10 Tuttle KR, Bruton JL, Perusek MC, Lancaster JL, Kopp DT, DeFronzo RA. Effect of strict glycemic control on renal hemodynamic response to amino acids and renal enlargement in insulin-dependent diabetes mellitus. N Engl J Med. 1991;324(23):1626-32. doi:10.1056/NEJM199106063242304
11 Krishna P, Kumar KP. Short-term effects of protein loading on urinary albumin excretion in Type 1 diabetic children with normoalbuminuria. Ind J Nephro. 2003;13(2):59-63. doi:10.4103/0971-4065.34869
12 Ikizler TA, Burrowes JD, Byham-Gray LD, et al. KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update. Am J Kidney Dis. 2020;76(3 Suppl 1):S1-S107. doi:10.1053/j.ajkd.2020.05.006
13 Azevedo MJ, Padilha LM, Gross JL. A short-term low-protein diet reduces glomerular filtration rate in insulin-dependent diabetes mellitus patients. Braz J Med Biol Res. 1990;23(8):647-54.
14 Dullaart RP, Beusekamp BJ, Meijer S, van Doormaal JJ, Sluiter WJ. Long-term effects of protein-restricted diet on albuminuria and renal function in IDDM patients without clinical nephropathy and hypertension. Diabetes Care. 1993;16(2):483-92. doi:10.2337/diacare.16.2.483
15 Koya D, Haneda M, Inomata S, et al. Long-term effect of modification of dietary protein intake on the progression of diabetic nephropathy: a randomised controlled trial. Diabetologia. 2009;52(10):2037-45. doi:10.1007/s00125-009-1467-8
16 Nezu U, Kamiyama H, Kondo Y, Sakuma M, Morimoto T, Ueda S. Effect of low-protein diet on kidney function in diabetic nephropathy: meta-analysis of randomised controlled trials. BMJ Open. 2013;3(5):e002934. doi:10.1136/bmjopen-2013-002934

Received*: 28-02-2026 -* ***Accepted****: 26-04-2026 -* ***Published****: 02-05-2026*

17 Pfeiffer AFH, Pedersen E, Schwab U, Risérus U, Aas A-M, Uusitupa M, et al. The Effects of Different Quantities and Qualities of Protein Intake in People with Diabetes Mellitus. Nutrients. 2020;12(2):365. doi:10.3390/nu12020365
18 Pan Y, Guo LL, Jin HM. Low-protein diet for diabetic nephropathy: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2008;88(3):660-6. doi:10.1093/ajcn/88.3.660
19 Yan B, Su X, Xu B, Qiao X, Wang L. Effect of diet protein restriction on progression of chronic kidney disease: A systematic review and meta-analysis. PLoS One. 2018;13(11):e0206134. doi:10.1371/journal.pone.0206134
20 Maroni BJ, Steinman TI, Mitch WE. A method for estimating nitrogen intake of patients with chronic renal failure. Kidney Int. 1985;27(1):58-65. doi:10.1038/ki.1985.10
21 Kesteloot H, Joossens JV. On the determinants of the creatinine clearance: a population study. J Hum Hypertens. 1996;10(4):245-9.
22 Pijls LT, de Vries H, Donker AJ, van Eijk JT. The effect of protein restriction on albuminuria in patients with type 2 diabetes mellitus: a randomized trial. Nephrol Dial Transplant. 1999;14(6):1445-53. doi:10.1093/ndt/14.6.1445
23 The EUCLID Study Group. Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normoalbuminuria or microalbuminuria. Lancet. 1997;349(9068):1787-92. doi:10.1016/S0140-6736(96)10244-0
24 Premen AJ. Protein-mediated elevations in renal hemodynamics: existence of a hepato-renal axis? Med Hypotheses. 1986;19(3):295-309. doi:10.1016/0306-9877(86)90077-0
25 Fontana L, Weiss EP, Villareal DT, Klein S, Holloszy JO. Long-term effects of calorie or protein restriction on serum IGF-1 and IGFBP-3 concentration in humans. Aging Cell. 2008;7(5):681-7. doi:10.1111/j.1474-9726.2008.00417.x
26 Zhu HG, Jiang ZS, Gong PY, et al. Efficacy of low-protein diet for diabetic nephropathy: a systematic review of randomized controlled trials. Lipids Health Dis. 2018;17(1):141. doi:10.1186/s12944-018-0791-8
27 Raal FJ, Kalk WJ, Lawson M, et al. Effect of moderate dietary protein restriction on the progression of overt diabetic nephropathy: a 6-mo prospective study. Am J Clin Nutr. 1994;60(4):579-85. doi:10.1093/ajcn/60.4.579
28 Velázquez López L, Sil Acosta MJ, Goycochea Robles MV, Torres Tamayo M, Castañeda Limones R. Effect of protein restriction diet on renal function and metabolic control in patients with type 2 diabetes: a randomized clinical trial. Nutr Hosp. 2008;23(2):141-7.
29 Hansen HP, Tauber-Lassen E, Jensen BR, Parving HH. Effect of dietary protein restriction on prognosis in patients with diabetic nephropathy. Kidney Int. 2002;62(1):220-8. doi:10.1046/j.1523-1755.2002.00421.x
30 Pan Y, Guo LL, Jin HM. Low-protein diet for diabetic nephropathy: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2008;88(3):660-6. doi:10.1093/ajcn/88.3.660
31 Riccardi G, Rivellese AA. Effects of dietary fiber and carbohydrate on glucose and lipoprotein metabolism in diabetic patients. Diabetes Care. 1991;14(12):1115-25. doi:10.2337/diacare.14.12.1115
32 Hagander B, Asp NG, Efendić S, Nilsson-Ehle P, Scherstén B. Dietary fiber decreases fasting blood glucose levels and plasma LDL concentration in noninsulin-dependent diabetes mellitus patients. Am J Clin Nutr. 1988;47(5):852-8. doi:10.1093/ajcn/47.5.852
33 Laakso M, Uusitupa M, Takala J, Majander H, Reijonen T, Penttilä I. Effects of hypocaloric diet and insulin therapy on metabolic control and mechanisms of hyperglycemia in obese non-insulin-dependent diabetic subjects. Metabolism. 1988;37(11):1092-100. doi:10.1016/0026-0495(88)90074-1
34 Ravid M, Brosh D, Ravid-Safran D, Levy Z, Rachmani R. Main risk factors for nephropathy in type 2 diabetes mellitus are plasma cholesterol levels, mean blood pressure, and hyperglycemia. Arch Intern Med. 1998;158(9):998-1004. doi:10.1001/archinte.158.9.998
35 Raja P, Maxwell AP, Brazil DP. The Potential of Albuminuria as a Biomarker of Diabetic Complications. Cardiovasc Drugs Ther. 2021;35(3):455-66. doi:10.1007/s10557-020-07035-4

Received: *28-02-2026* - ***Accepted***: *26-04-2026* - ***Published***: *02-05-2026*