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Regular paper

Impact of diet modification on body mass and kidney function in patients with diabetic nephropathy: a pilot study

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Objectives: The increasing trend in chronic kidney disease (CKD) has occurred in parallel with the increased prevalence of obesity and diabetes type 2. The relationship between a reduction in body mass and protein intake in diabetic nephropathy (DN) has not been adequately understood. This study aimed to determine whether dietary intervention in an adult with DN is associated with decreasing proteinuria or changes in kidney function over six months. Methods: The study included 120 patients with DN, consecutively admitted to a dietitian from a Kidney Disease Clinic. Patients were classified into two groups: a reduction diet or a normal calorie diet, both with 0.8 g of protein/kg of ideal body weight/day. Anthropometric and laboratory assessments were done before and after observation. Results: After six months, in the study group of patients on a reducing diet, a decrease in body mass, body mass index (BMI) and stabilization of estimated glomerular filtration rate (eGFR) were observed. There was also a significant correlation between the time of diabetes diagnosis and eGFR and creatinine (R Spearman=–0.24 and 0.3, respectively; *p*=0.05). There were no other significant associations between body mass, BMI, albuminuria, eGFR, or creatinine. Conclusions: The study shows that obesity is a common comorbid disease in patients with DN and that dietary intervention is associated with a significant reduction in body mass and stabilization of eGFR in these patients.

Keywords: diet; obesity; diabetes; diabetic nephropathy; estimated glomerular filtration rate

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Abbreviations: BMI, body mass index; BMR, basal metabolic rate; CC, creatinine clearance; CKD, chronic kidney disease; DN, diabetic nephropathy; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HbA1c, glycated hemoglobin/hemoglobin A1c; TDEE, total daily energy expenditure; UACR, urine albumin-to-creatinine ratio

INTRODUCTION

Diabetic nephropathy (DN), also known as diabetic kidney disease is one of the most common complications of diabetes and is the leading cause of end-stage kidney disease (ESKD) in the general population (Khan *et al.,* 2018). DN is characterized by the development of progressive albuminuria and the loss of the glomerular filtration rate (GFR) (Tutle *et al.,* 2014). Published studies have shown that among patients who started renal replacement therapy, the percentage of patients with diabetes (only DN) ranged from 24% to 51% (all causes were counted) and is still increasing (Buyadaa *et al.,* 2020).

According to the World Health Organization (WHO), the number of patients requiring renal replacement therapy is expected to double by 2030 (Luyckx *et al.,* 2018). Therefore, conservative treatment of chronic kidney disease (CKD) is becoming increasingly important from the point of view of preventing an epidemic of this disease. Experts point to the importance of proper dietary management and education in this area as one of the key points in the development of nephroprotective effects, which may have a measurable, positive impact on the quality of life of patients and inhibit the increase in the number of patients at the end-stage of the disease (Tutle *et al.,* 2014).

The main cause of excess body weight and its complications are lifestyle changes, limitation of physical activity, improper eating habits, and above all, the excessive consumption of high-energy products (Swinburn *et al.,* 2004). Changing incorrect eating habits is most effective in the early stages of diseases such as obesity, diabetes type 2, or CKD, but at every stage it is worth recommending that patients correct any eating mistakes. However, the relationship between overweight or obesity in patients with CKD and the mortality risk is not clear. Dietary intervention is particularly important in patients with CKD, as well as in other disease states and metabolic phenotypes such as obesity and diabetes, which affect the risk of developing and exacerbating the progression of CKD (Díaz-López *et al.,* 2021).

Treatment of DN includes intensive control of glycemia – glycated hemoglobin/hemoglobin A1c (HbA1c) <7%, proteinuria, hypertension through pharmacotherapy, as well as lifestyle modifications. The American Diabetes Association (ADA) recommendations for people with DKD do not promote a change in the amount of protein in the diet below 0.8 g/ kg/ day but rather suggest replacing the animal protein source with soybean to reduce cardiovascular risk (American Diabetes Association, 2014). Moreover, the latest recommendations of NKF KDOQI Clinical Practice Guideline On Nutrition In CKD: 2020 Update (Ikizler *et al.,* 2020) indicate the possibility of limiting protein consumption in the range of 0.6–0.8 g/kg/ day in the group of adults with diabetes and with estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2. The study aimed to determine whether dietary intervention in an adult with DN is associated with proteinuria or changes in kidney function during a six-month observation period.

MATERIAL AND METHODS

Study design

The current study was a 6-month interventional study to determine the effects of dietary intervention on renal function and proteinuria in adults with DKD. The nephrologist enrolled DKD patients in the study and referred them to a clinical dietitian. The dietitian then wrote down the rules of the diet and, based on the body mass index (BMI), divided patients into two groups. Dietitian visits were scheduled every 4–6 weeks, and nephrological control visits every 12 weeks.

DKD was diagnosed in patients with diabetes according to recommendations: if indicators of kidney damage persist ≥3 months:

– macroalbuminuria – urine albumin-to-creatinine ratio (UACR) >300 mg/g)

– microalbuminuria – 30–300 mg/g in the presence of diabetic retinopathy; in diabetes type 1 (additionally), when the duration of the disease is at least ten years (KDOQI, 2007).

Inclusion criteria for the study were: age >18 years old, DKD stages 2–5, good nutritional status, and signed consent to participate in the study.

All subjects gave informed consent to the inclusion before participating in the study. The study was approved by the Bioethical Committee.

Initially, 120 patients were enrolled in the study, but 50 (42%) were excluded because they did not follow the diet and did not attend follow-up visits. The scheme of the study is presented in Fig. 1.

Study population

Ultimately, the study population consisted of 70 clinically stable patients with DKD, at an average age of 65.1±11.8 years, admitted to the dietitian from the ambulatory Department of Nephrology, Transplantology and Internal Medicine at the University Clinical Center in Gdansk (Poland) in the years 2018–2020.

The results were collected over six months of follow-up, with visits every 1–3 months. At each visit, body weight, laboratory parameters and compliance with dietitian rules were assessed.

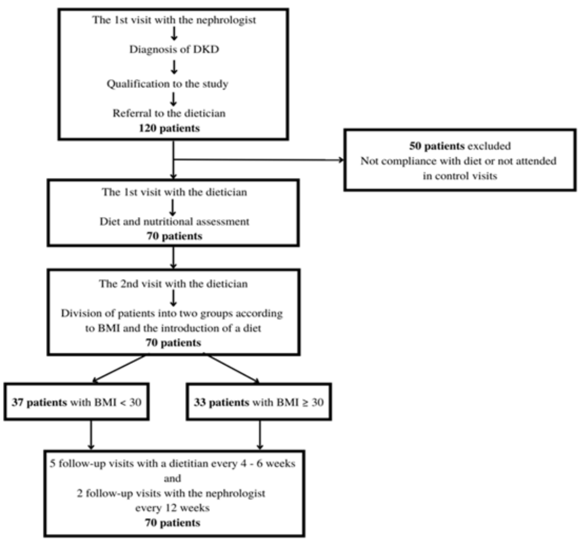

Figure 1. Scheme of the study.

Dietary intervention

All patients who consented to participate in the study had a personal appointment with a dietitian with extensive experience in the management of CKD diet. Diet planning methodology included the determination of energy demand by measuring basal metabolic rate (BMR) based on bioimpedance mass indications. The patient's total daily energy expenditure (TDEE) was then calculated using the appropriate level of physical activity (PAL):

– 1.4 – for people with low physical activity,

– 1.6 – for people with medium physical activity,

– 2.0 – for people with high physical activity.

Protein intake was established at 0.8 g/kg of ideal body weight/day, phosphorus 800-1200 mg/day and potassium 2000–2500 mg/ day. The ideal body weight is calculated based on Broc's formula.

Patients with BMI ≥30 were qualified for the reduction diet – the amount of body weight loss per unit time was set at 0.5–1.0 kilograms per week – to unify the deficit of 500 kcal/day. Patients with BMI <30 were enrolled in a normal calorie diet.

The following nutrient requirements were determined in both groups: protein – 0.8 g/kg of ideal body weight/day, carbohydrates – 45-55% and fats – 30–35% of daily energy requirement. The mineral demand was determined based on the dietary standards of the Polish population. The patients' daily diet is defined as 4–5 meals. During the observation, patients met with a dietitian to obtain nutritional advice. At each control meeting, a 24-hour diet recall was conducted, and patients were asked to record their diet for three days before the visit. Patients were re-educated on the correct application of the diet. Each time during the meeting, patients were subjected to bioimpedance measurements, based on which BMR and TDEE were determined as the starting point for determining energy reduction in the diet, in accordance with the recommendations of the Polish Society of Dietetics and NKF KDOQI (KDOQI, 2007; Gajewska *et al.,* 2015). All patients were instructed to maintain a minimum level of 150 min. per week of physical activity throughout the study period.

BMI

Measurement of body mass with the scale (Tanita BC 420) was performed at each visit by a dietitian. The BMI was calculated using the following formula: BMI=body weight/height^2 (kg/m^2). The BMI classification was adopted: <18.5 – underweight; 18.5–24.9 – normal body weight; 25.0–29.9 – overweight; ≥30.0 – obesity. The ideal body weight was calculated according to Broc's formula (height in cm –100); height was measured in a stadiometer.

Laboratory Measurements

Albumin, triglycerides, total cholesterol, phosphorus, potassium, creatinine, fasting glucose, HbA1c, and blood counts were measured for all participants (baseline and at six months) using routine laboratory tests. UACR was calculated from urine albumin and creatinine. eGFR was calculated according to The Modification of Diet in Renal Disease (MDRD) equation and creatinine clearance (CC) was obtained from The Cockroft-Gault equation. After three months of observation, serum creatinine

Table 1. Basic characteristics of the studied patients.

Parameters	All patients with DN n=70
Age (years)	65.1±11.8 (40–87)
M/F	40/30
BMI (kg/m²)	30.4±7.3 (18.4–53.1)
eGFR (ml/min/1.73 m²) acc. MDRD	41.3±20.5 (8.0–123)
CC (ml/min.) acc. Cockroft -Gault	60.2±50.5 (8.6–260.0)
Creatinine (mg/dl)	2.0±1.1 (0.6–6.6)
Time since diagnosis of diabetes (years)	9.8±4.8 (4–18)
HbA1c (%)	6.6±1.1 (6.3–7.5)
Stage of CKD	
G2 (%)	11.5
G3 (%)	62.8
G4 (%)	17.1
G5 (%)	8.6

Data are presented as mean ± S.D. and range Aberrations: M, men; F, female; BMI, body mass index; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; CC, creatinine clearance; HbA1c, glycated hemoglobin/hemoglobin A1c; CKD, chronic kidney disease

and UACR were measured. All patients performed self-monitoring of blood glucose and blood pressure during follow-up.

Statistical Analysis

Results are expressed as percentages (for categorical variables), mean, and standard deviation. The assumption of normality was verified by the Kolmogorov-Smirnov test. A *p*-value <0.05 was considered statistically significant. The Spearman correlation coefficient (R) was used to assess the correlation between the assessed variables. Comparisons between the two groups were assessed using the Student's *t*-test or the U-Mann–Whitney test, respectively. The change in value between the first visit and the last visit (value for the last visit minus the value for the first visit) was compared between the groups. The comparison was made using the Wilcoxon test. Statistical processing of the results was performed with the use of the statistical software STATISTICA PL v 13.0 (Statsoft, Kraków, Poland).

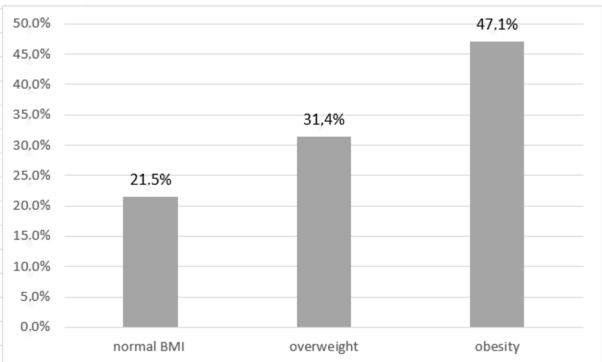

Figure 2. The percentage of patients with excess body mass at baseline.

RESULTS

Characteristics of patients with DN

The results of 70 patients who completed the study were analyzed. The baseline patient characteristics are shown in Table 1. Diabetes type 1 was diagnosed among 11 patients (15%), and diabetes type 2 among 59 (85%). The mean duration of diabetes was 9.84 ± 4.8 years (range 4–18).

There were five obese patients in the G2 stage, G3 had 22 patients, G4 had four patients, and G5 had two patients. Most of the patients were treated with insulin, and 43% received oral antidiabetic drugs from various groups. Antihypertensive treatment with renin-angiotensin system blockers was received by 97% of patients.

Baseline results

A total of 33 patients (47.1%) were obese; 22 (31.4%) were overweight, and 15 (21.5%) presented normal BMI at baseline (Fig. 2).

The mean serum albumin level was 38.2±2.9 mg/L and indicated good nutritional status in patients. Serum levels of potassium and phosphorus were in reference ranges (4.6±0.6 mmol/L; 3.9±0.9 mg/dL, respectively). The mean fasting glucose level was 149.06±54.0 mg/dL and HbA1c – 6.6%. The mean eGFR was 41.3±20.5 mL/min/1.73 m² and the mean CC, according to the Cockroft-Gault formula, was 60.2±50.5 mL/min. The correlation between eGFR MDRD and CC was high (R=0.88; *p*<0.05). The UACR was in the range of 1120±152 mg/g.

In addition, a statistically significant correlation between the time of diabetes diagnosis and eGFR and creatinine (R Spearman=–0.24 and 0.3, respectively; *p*=0.05) was noted. There was no significant relationship between body mass, BMI, albuminuria, eGFR, CC and serum creatinine.

Follow-up results

As presented in Table 2, in the study group, after six months of dietary intervention, a decrease in body mass and BMI was noted in comparison to the baseline parameters. Serum creatinine, eGFR, UACR, albumin, phosphorus, and potassium were changed insignificantly. Changes in eGFR are presented in Fig. 3.

In the obese group, the mean body weight loss over six months was 7.0±2.2 kg, and in the non-obese group,

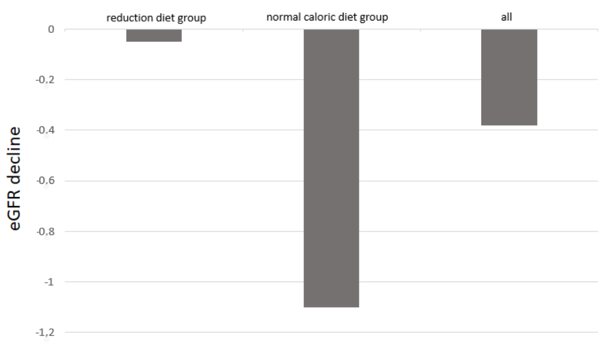

Figure 3. Changes in eGFR according to used diet.

Table 2. The anthropometric and biochemical parameters in patients before and after 6 months of dietary intervention.

Parameters	All n=70 before	All n=70 after	Obese group n=33 before	Obese group n=33 after	Non-obese group n=37 before	Non-obese gro-up n=37 after
Body Mass (kg)	93.8±26.5	89.6±28.7	110.3±20.8	102.4±29.5	71.2±13.5	70.8±13.5
BMI (kg/m^2)	30.4±7.3	29.0±8.2	36.0±6.3	34.0±6.2	25.3±3.4	24.6±5.3
Albumin (g/L)	38.2±2.9	37.1±3.1	37.0±2.7	35.0±1.6	38.7±3.0	37.1±2.1
Phosphorus (mg/dL)	3.9±0.9	3.5±7.4	3.8±0.7	3.5±0.6	4.7±1.7	4.6±2.6
Potassium (mg/dL)	4.6±0.6	4.8±0.9	4.47±0.7	4.5±0.56	4.8±1.9	4.9±2.0
eGFR (ml/min/1.73 m^2) acc. MDRD	41.3±20.5	36.9±2.5	42.8±22.2	42.7±19.7	40.0±19.0	39.4±17.8
Creatinine (mg/dL)	2.0±1.1	2.2±1.3	1.88±9.1	2.06±1.1	2,17±1.5	2.2±2.1
CC (mL/min) acc. Cockroft-Gault	60.2±50.2	50.1±41.1	80.2±61.7	60.2±43.8	42.7±29.2	40.8±30.1
Hemoglobin (g/dL)	12.9±1.6	12.7±1.9	11.9±1.7	11.8±1.9	12.9±2.2	13.4±2.4
Total cholesterol (mg/dL)	214.4±50.5	198.2±37.8	231±47	221±57	231±45	235±67
HDL (mg/dL)	48.2±14.0	48.9±12.6	43.5±11.4	46.1±13.6	37.8±7.9	38.9±11.1
HbA1C (%)	6.8±1.1	6.7±0.8	6.8±1.2	6.9±1.3	6.8±2.4	6.6±2.1
Glucose fasting (mg%)	148±48	132±54	156±68	143±59	145±87	156±50
UACR (mg/g creatinine)	1120±152	1525.5±120.8	2290±187	2131±213	1241±256	1820±252

Data are presented as mean ±S.D. Aberrations: BMI, body mass index; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; CC, creatinine clearance; HDL, high-density lipoprotein; HbA1c, glycated hemoglobin/hemoglobin A1c; UACR, urine albumin-to-creatinine ratio

it was 0.4±0.4 kg. The urinary protein excretion in both groups did not change significantly.

DISCUSSION

The occurrence of excess body mass in DN patients and the effectiveness of six months of dietitian intervention were observed in the study. The prevalence of obesity was 47%, and about 31% of the patients were overweight. After six months of the reduction diet, 63.6% of patients decreased their body mass and BMI. Excess weight is often associated with type 2 diabetes. Moreover, the accumulation of adipose tissue in the trunk area in patients with type 2 diabetes may be associated with potential consequences, for instance, albuminuria, proteinuria, and a decrease in GFR (Gnacińska *et al.,* 2009). Mild renal failure is associated with high cardiovascular risk in the general population: any decrease in eGFR below the norm of 5 mL/min increases cardiovascular risk by 26% (Schram *et al.,* 2004; Ronald *et al.,* 2002). Serum creatine concentrations >1.6 mg/dL are associated with a 20% increased risk of mortality for all causes, cardiovascular and ischemic cardiovascular conditions (Wannamethee *et al., 1997).*

The presented results confirm that obesity is a major public health problem among diabetic patients, including those with DN. The prevalence of excess body mass reached 80%, which indicates that a significant number of patients in nephrology outpatients required appropriate nutritional treatment (Bijelic *et al.,* 2020). It is also worth emphasizing that a significant number of patients (50/120, 42%) did not agree with the proposed diet, which is a significant problem in clinical practice. However, in the obese group, about 36% of patients did not lose significant body weight, possibly due to non-compliance with the diet. The resignation from dietitian intervention was more frequent in the beginning – perhaps more accurate education is needed among patients with diabetes. Despite recommendations for lifestyle modification at every stage of diabetes, patients were not co-operative.

In the current study, a diet of 0.8 g protein/kg ideal body weight/day was followed as recommended. Additionally, in obese patients, a caloric deficit of 500 kcal/day was established. The primary goal of the diet was adequate glycemic control, as measured by self-measured fasting glucose and HbA1c. In the current study, the average level of HbA1c was 6.8% and did not change throughout the observation. The second goal was to reduce body weight in obese patients and to establish an association between weight loss and eGFR, CC, and proteinuria. It is well known that a properly balanced diet allows for a sustained reduction in body weight by an average of 0.5-1 kg per week (Bray *et al.*, 2003; Sacks *et al.*, 2009; Hruby *et al.*, 2015).

In the current study, the mean weight loss in obese patients (BMI>30) was approximately 7 kg/6 months. Despite a weight loss of about 1 kg per month, no statistically significant changes were found in eGFR, CC or albuminuria. The average decrease in eGFR in the study was 0.37 mL/min/1.73 m^{2,} and satisfactory and stable results were obtained. The observed decrease in CC from 80.2–60.2 mL/min in the obese group is favorable because it indicates a decrease in hyperfiltration and also indicates that eGFR, according to MDRD, is a less accurate parameter, especially in obese people. Navanethan S.D. and others showed in a meta-analysis that weight loss as a result of dietary or bariatric intervention is associated with a reduction in proteinuria, blood pressure and, in the case of severe obesity, with normalization of eGFR (Navaneethan *et al.,* 2009). Moreover, Diaz-Lopez et al., in the PREDIMED-Plus trial, concluded that the lifestyle intervention approach may preserve renal function and delay CKD progression in adults with excess body mass (Diaz-Lopez *et al.*, 2021). The RIGOR-TMU study also indicated that weight loss after bariatric surgery was associated with eGFR preservation in patients with CKD (Becerra-Tomás *et al.,* 2019).

The ADA published a nutrition care model that provided evidence-based, standardized, high-quality care for non-dialyzed patients with CKD. The document reported that: "nutrition care provided by a registered dietitian up to twice monthly over one year can have a valuable role in the medical care of patients with CKD by providing nutrition assessment and interventions to delay kidney disease progression in addition to co-morbid conditions, such as diabetes, cardiovascular disease (CVD), dyslipidemia, gout, and nephrolithiasis" (American Diabetes Association. Choose Your Foods, 2014). In the current study, follow-up visits were established every 4-6 weeks, while in everyday practice, meetings with dietitians are less frequent. The effectiveness of diet modification might be better if the ADA recommendations were applied in both research and practice.

The primary goal of diabetes treatment is to maintain optimal glycemic control and to prevent complications, including renal and cardiovascular complications. The NKF KDOQI recommendations from 2020 focus on dietary protein intake as a factor in the progression of kidney damage and suggest 0.6–0.8 g of protein/kg/day in adult patients with diabetes and CKD stages 3–5. The NKF KDOQI recommendations are based on expert opinion and must be used with caution, i.e., only in patients in good clinical condition, in good nutritional status, and cooperating well, otherwise, there is a risk of malnutrition (Ikizler *et al.,* 2020). In the current study, despite 0.8 g of protein/kg of ideal body weight/per day, there was a tendency to lower the level of albumin.

The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines suggest a more liberal diet when protein intake is 0.8 g/kg body weight per day and does not exceed >1.3 g of protein/kg body weight (Avesani *et al.,* 2005). KDIGO guidelines underline that reducing protein intake is associated with slowing the progression of CKD, improving urea and phosphate levels, and reducing acidosis (Cupisti *et al.;* 2020). However, some studies have shown that low-protein diets reduce hyperfiltration (Kontessis *et al.,* 1990; De Nicola *et al.,* 2020).

In the second studied group (on a normal calorie diet with 0.8 g of protein/kg/day), changes were not noted in any body mass, eGFR, or UACR during the observation period, and the dietitian's assessment indicated good adherence to the recommendations in this group. In the study, a diet based on animal and plant products was used, but there are reports that plant protein is more beneficial in CKD. Some authors (McGraw *et al.,* 2016; Moorthi *et al.,* 2017) have suggested that plant-based diets are more beneficial for DKD patients, especially those with high cardiovascular risk.

In everyday practice, it is very important to correct a patient's diet. It should be noted that not only the supply of protein is important, but also the content of calories, fat, and carbohydrates as well as vitamins and minerals (Skrypnik *et al.*, 2019). The ADA recommends lifestyle modifications based on increased physical activity and the assumptions of the Mediterranean or DASH diet, reducing the consumption of saturated fatty acids and trans isomers and increasing fiber and unsaturated fatty acids (American Diabetes Association. Choose Your Foods, 2014).

The authors would like to emphasize the need to educate patients and medical staff in the field of primary and secondary prevention. Proper modification of the diet is recommended by nephrological societies in delayed kidney dysfunction and is also recommended as prophylaxis of cardiovascular events (Skrypnik *et al.,* 2019; Skrypnik *et al.*, 2020). The current results suggest the advantages of including simultaneous pharmacological and dietary intervention in the overall prevention of ESKD and cardiovascular risk in patients with excess body weight and diabetic nephropathy. To draw more precise conclusions, more research is needed on the effects of weight loss and modification of protein intake on the progression of CKD in obese patients with DN.

LIMITATIONS OF THE STUDY

The current study has several limitations. The first limitation is the small group of patients. Other limitations include the lack of detailed diet analysis and strict control of diet compliance, e.g., by the excretion of urea nitrogen in the urine. The observation time was short, and long-term studies are needed to analyze the renal outcomes, such as the development of renal dysfunction.

The strengths of the study include the demonstration of the role of a dietitian in the treatment of patients with diabetes and kidney diseases and the need to educate patients on non-pharmacological methods of treatment.

CONCLUSION

The study shows that obesity is a common symptom in patients with DN, and dietary intervention is associated with a significant reduction in body weight and stabilization of eGFR in these patients. As the majority of DN patients are at risk of obesity-related mortality, the advice of a dietitian should become part of both routine clinical evaluation and intervention.

PRACTICAL APPLICATION

The study shows the effect of dietary interventions on the progression of DN. The study also emphasizes that it is necessary to educate patients on the impact of diet on the progression of the underlying disease and the risk of complications, especially cardiovascular-related ones.

Declarations

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Author Contributions: Conceptualization, A.D-Ś., S.M.; methodology, M.K., and S.M.; validation, M.K.; formal analysis, S.C.-S., S.M.; investigation, M.K., M.S-W.; resources, M.K.; S.C.-S.; data curation, M.K., M.S-W; writing – original draft preparation, M.K., S.M.; writing – review and editing, S.C.-S., M.K., S.M.; supervision, M.C., A.D-Ś., and S.M. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Independent Bioethical Committee of the Medical University of Gdańsk (NKBBN/343/2018).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

Acknowledgments: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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