THE DIAGNOSIS OF DIABETIC KIDNEY DISEASE; FREQUENCIES OF URINARY MICROALBUMIN AND CREATININE RATIOS, AND THE ESTABLISHMENT OF CAUSAL RELATIONSHIPS BETWEEN LIPID AND GLYCEMIC LEVELS AND OBESITY IN AN ALGERIAN POPULATION

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ABSTRACT

Introduction*: Diabetic nephropathy (DN) is an insidious disease and is the leading cause of renal failure in diabetic patients. The main objective of this study was the early diagnosis of DN in at-risk individuals, using urinary albumin excretion to establish associations between glycemic balance, dyslipidemia, and renal involvement.*

Methods*: This prospective study included 292 patients with type 1 and 2 diabetes (T1D and T2D). Microalbuminuria was assessed using urinary microalbumin and creatinine ratios, assessed from the same first-morning urine sample. A glycated hemoglobin (EHbA1c) assay and lipid balance were also performed.*

Results*: The cohort had an average age of 55±15.9 years and a sex ratio of 0.67. Of the 292 patients, 35.3% were positive for microalbuminuria. A linear regression model showed a strong correlation between microalbuminuria and glycemic imbalance, total cholesterol, triglyceride, low-density lipoprotein (LDL-cholesterol), systolic blood pressure (SBP), and blood pressure diastolic (DBP), however, the chi-square test (X2) showed a negative association with the absence of microvascular complications (retinopathy and neuropathy) in type 1 diabetics. In type 2 diabetics, the linear regression model showed a positive relationship between microalbuminuria and EHbA1c, SBP, DBP, body mass index (BMI), abdominal perimeter, and lipid balance. While the chi-square (X2) test showed strong links between microvascular complications, smoking, alcohol consumption, high blood pressure (BP), and microalbuminuria, more detailed logistic regression analyses revealed associations between microalbuminuria and poorly balanced EHbA1c, systolic blood pressure (SBP), and disturbances in the balance sheet of HDL-cholesterol only.*

Conclusions*: DN appeared to be strongly correlated with poor glycemic control and disturbances in lipid profiles, suggesting dietary and improved medical control are important parameters for this condition.*

Keywords: *diabetic nephropathy, microalbuminuria, urine creatinine, microvascular complications, high blood pressure, lipid profile.*

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Introduction

Globally, diabetes prevalence is increasing, making it a public health concern. Disease severity and complications mainly affect the eyes, kidneys, nerves, heart, and blood vessels[1-3]. Diabetic nephropathy (DN) is the main cause of end-stage renal disease due to its insidious onset[4-6]. In some cases, 30 years can pass between an initial diabetes diagnosis and irreversible end-stage renal disease[7,8]). The condition is particularly feared by diabetics, not least because it can lead to dialysis (or kidney transplantation) and an increased risk of cardiovascular complications and death[9].

The main objective of clinical medicine is the early detection of DN in people at risk. This is performed by assessing urinary albumin excretion, which reflects potential kidney damage during DN.

Secondarily, establishing a relationship between glycemic balance, dyslipidemia, and the degree of renal impairment in diabetics in the Wilaya of Constantine (eastern Algeria). Also, analyzing the influence of hypertension (hypertension), obesity, smoking, and alcohol consumption on the occurrence and progression of DN and identify which of these factors is the most discriminatory.

We performed a prospective epidemiological study on 292 diabetics from the Wilaya of Constantine (eastern Algeria). The study was performed on the first-morning urine sample. Subjects not showing proteinuria by test strips, had blood tests to measure glycated hemoglobin (EHbA1c), triglycerides, total cholesterol, low-density lipoprotein (LDL-cholesterol) and high-density lipoprotein (HDL-cholesterol), and renal tests to measure urinary creatinine and urinary microalbumin. The study sought to answer the following question: will kidney disease in diabetics depend on the parameters taken into account?

Materials and methods

Study area

We performed an analytical and descriptive prospective epidemiological study over one year at diabetic centers in Bellevue and Bab El Kantra dispensary in Wilaya of Constantine, Algeria. Any diabetic patient presenting for a medical check-up was asked to participate, provided certain criteria were met. The study was performed with ethical agreement from these centers.

Study design and patients

All enrolled patients had been previously diagnosed with type 1 or type 2 diabetes mellitus (T1D and T2D). The study population was made up of 292 among which 117 men and 175 women, T1D (14-43 years of age) and with greater seniority in diabetes or equal to 5 years and T2D (36-86 years). Patient information was collected by validated questionnaire comprising: general information, pathological history (e.g. high blood pressure), smoking and alcohol consumption, clinical examination (e.g. height, weight, abdominal perimeter, body mass index (BMI), and microvascular complications, (e.g. retinopathy or neuropathy). Patient consent was obtained prior to the collection of personal data. Pregnant women and diabetic patients with the following pathologies were excluded; non-hypertensive heart disease, liver disease, and other kidney diseases, urinary tract infections or hematuria, acute infection (fever), and proteinuria as detected by test strips.

Study participant clinical characteristics

Blood pressure (BP) was measured in a sitting position after 15 minutes of rest, using an Omron M3 (Eskisehir, Turkey) automatic BP monitor fitted with an adult cuff. BP was recorded twice. The monitor displayed systolic blood pressure (SBP), blood pressure diastolic (DBP), and pulse rates. Anyone with a BP > 140/90 mm Hg was considered hypertensive (10). Patient weights were measured using a Camry EB9003 electronic scale (Hubei, China). The Abdominal perimeter was measured using conventional methods, measurements not exceeding 102 cm were considered normal in men, and for women, the limit was 88 cm. BMI was calculated using the formula: BMI = weight (kg)/ height (m^2). This parameter assessed subject size. Patients were separated according to BMI: normal, overweight, and obese, to assess if obesity influenced DN onset and its progression.

Blood and urine sample collection and storage

Two 5 ml blood samples for each subject (heparin and complexion) were taken, generally at the elbow, after a night of fasting. Sampling was performed by center nursing staff between 7 am and 7.30 am. Subjects were provided with dry tubes (without preservatives) to collect the first urine sample of the day. Samples were refrigerated and transported to the biochemistry laboratory of Constantine University Hospital Center, where they were either processed within the hour or stored at 4°C until required.

Well, mixed blood samples were centrifuged at 3000 rpm for 10 min using a Nüve NF 800 centrifuge (Amazon, UK) to separate serum for chemistry analyses. Patient samples underwent glycemic assessment, including EHbA1c assay on a HPLC-D-JO (Bio-Rad, Marne-La-Coquette, France) the D-IO methodology Bio-Rad is certified NGSPIDCCT and IFCC, France. Other measurements included lipid balance, triglycerides, total cholesterol, HDL-cholesterol, and LDL-cholesterol using the Abbott ARCHITECT Ci 8200 (Bonney Lake, WA, États-Unis), and urinary creatinine and microalbuminuria (performed on urine). The microalbuminuria assay was performed using the Dimension Xpand Plus, Siemens analyzer (SIEMENS-BAYER, German), on morning urine. The urine was previously tested using

urine strips to assess for proteinuria or hematuria positivity (exclusion criteria); if positive for either, the urine was discarded, the reference method on 24-hour urine with poor reproducibility, in particular by incomplete urinary collection. This is why we used the first morning urine sample and expressed the results in relation to urine creatinine, by calculating albuminuria/creatininuria ratios.

The microalbumin assay method was based on a turbidimetric particle inhibition immunoassay (PETUNIA) technique[11], allowing direct quantification of albumin in the urine. During the 37°C reactions, an insoluble immunological urinary albumin complex was formed with a specific anti-albumin antibody. The rate of albumin aggregation to the antibody was inversely proportional to the albumin concentration in the sample. The reaction was measured at 340 nm and 700 nm by Dimension Xpand Plus, Siemens analyzer (SIEMENS-BAYER, German). Microalbuminuria concentrations derived from the urinary microalbumin/urinary creatinine ratio were calculated as follows: Microalbuminuria (μg/mg creatinine) = (microalbumin (mg/l) x 1000)/ urine creatinine (mg/l) A positive microalbuminuria result was considered with a ratio 22 μg/mg and normoalbuminuria (<0.2 μg/mg)[12].

Data Analysis

We performed descriptive analyses of socio-demographic, clinical, para-clinical, and therapeutic characteristics for all patients. The results were presented as percentages and as correlation coefficients (R). Percentages were compared using the chi-square test (X2), and coefficients using the Pearson correlation test were used to determine relationships between microalbuminuria and other quantitative factors (EHbA1c, BMI, abdominal perimeter, SBP, DBP, cholesterol, triglycerides, LDL-cholesterol, and HDL-cholesterol). Any differences were considered statistically significant at $p < 0.05$. All statistics were produced using IBM-SPSS for Windows, version 20 (SPSS, Inc., Chicago, IL). When a diabetic parameter was correlated to microalbuminuria using bivariate analysis, we tested the independence of this correlation by multivariate analysis (multiple logistic regression model).

Results

General characteristics of study participants

In this study, 86.3% of participants were type 2 diabetics; 40.06% were men, and 59.94% were women, representing a sex ratio of 0.67. The median age was 58 years, ranging from 14 to 86 years. The modal age group was 60-69 years (Table 1).

The population of type 1 diabetics included 60% of women. Among type 1 diabetics, 67.5% of participants were < 30 years (67.5%). The median age was 20 years, ranging from 14 to 43 years. The modal age group was 20-29 years (Table 1).

59.92% of women were type 2 diabetics. 96.43% of participants with T2D were > 40 years, the median age was with extreme ages 36 and 86 years, and the modal age group was 60-69 years. The modal class was: 5-28 years, the median duration of evolution was 11 years (Table 1).

Characteristics	N = 292 (100%)	
	T1D; 40 (13.70%)	**T2D; 252 (86.30%)**
Sex		
Male 117 (40.06 %)	16 (40 %)	101 (40.08 %)
Female 175 (59.94 %)	24 (60 %)	151 (59.92 %)
Age categories (years)		
10–19 12 (4.11 %)	10–19 12 (30 %)	30–39 9 (3.57 %)
20–29 15 (5.14 %)	20–29 15 (37.5 %)	40–49 34 (13.49 %)
30–39 20 (7 %)	30–39 11 (27.5 %)	50–59 78 (30.96 %)
40–49 36 (12.33 %)	40–49 2 (5 %)	60–69 81 (32.14 %)
50–59 78 (26.71 %)		70–79 42 (16.67 %)
60–69 81 (27.74 %)		80–89 8 (3.17 %)
70–79 42 (14.38 %)		
80–89 8 (2.74 %)		
Diabetes duration (years)	5–10 15 (37.5 %)	T2D duration was not considered
	10–15 10 (25 %)	
	15–20 9 (22.5 %)	
	20–25 3 (7.5 %)	
	≥ 25 3 (7.5 %)	
Obesity according to BMI		
Normal weight 78 (26.71 %)	14 (35 %)	64 (25.4 %)
Overweight 122 (41.78 %)	13 (32.5 %)	109 (43.25 %)
Obesity class I 62 (21.23 %)	8 (20 %)	54 (21.43 %)
Obesity class II 23 (7.87 %)	3 (7.5 %)	20 (7.94 %)
Obesity class III 7 (2.39 %)	2 (5 %)	5 (1.98 %)
Abdominal obesity		
Normal values		
Male 72 (24.66 %)	10 (62.5 %)	62 (61.39 %)
Female 40 (13.60 %)	1 (4.17 %)	39 (25.83 %)
High values		
Male 45 (15.41 %)	6 (37.5 %)	39 (38.61 %)
Female 145 (46.23 %)	23 (95.83 %)	112 (74.17 %)
Microvascular complications		
Yes 121 (41.43 %)	16 (40 %)	105 (41,67)
No 171 (58.86 %)	24 (60 %)	147 (58.33)
Smoking		
Yes 212 (72.60 %)	35 (87.5 %)	177 (70.29 %)
No 80 (27.40 %)	5 (12.5 %)	75 (29.71 %)
Alcohol intake		
Yes 154 (52.74 %)	22 (55 %)	132 (52.38 %)
No 138 (47.26 %)	18 (45 %)	120 (47.62 %)
High blood pressure		
Yes 99 (33.90 %)	10 (25 %)	89 (35.32 %)
No 193 (66.10 %)	30 (75 %)	163 (64.68 %)

Table 1: Socio-demographic participant characteristics.

Clinical characteristics of diabetic participants

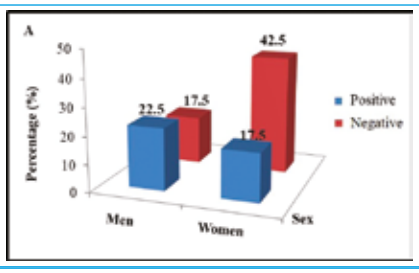
Study complications included retinopathy and neuropathy, 58.86% of participants were unharmed. 60% were type 1 diabetics were with retinopathy or neuropathy, or both simultaneously. BMI indices for type 1 diabetics ranged from 19.71-69.09 kg/m2, the median was 26.97 kg/m^2. In total, 65% of subjects were obese, to differing degrees (obesity to very severe obesity). 35% had a normal BMI. 23% of type 1 diabetics had abdominal obesity, most of whom were women. The extremes ranged from 51–115 cm and the median was 110.5 cm. 87.5% of type 1 diabetics were smokers and 55% confirmed

taking alcohol. 75% of type 1 diabetics were not hypertensive (Table 1).

41.67% were T2D with complications. 74.6% with type 2 diabetics presented with obesity, to differing degrees (obesity to very severe obesity), versus 25.4% with a normal BMI. BMI indices for type 2 diabetics ranging from 18.06 kg/m2–69.09 kg/m2, their median was 27.19 kg/m2. 59.92% of type 2 diabetics suffered with abdominal obesity, most of whom were women, and measures varied between 50 cm and 132 cm, with a median of 100 cm. 70.29% of type 2 diabetics were smokers and 52.38% confirmed alcohol consumption. 35.32% of type 2 diabetics suffered from high BP (Table 1).

Laboratory markers in diabetic patients

40% of T1D patients had microalbuminuria (Fig. 1). 60% subjects had glycated hemoglobin A1c ≤ 7% (balanced diabetics), these values varied between 4.1% and 16.55% and the median was 6.3%. 60% of participants with T1D had normal cholesterol values, with a median of 2.19 g/l. 60% of type 1 participants had normal triglyceride levels; values varied between 0.39 and 4.57 g/l, and the median was 1.25 g/l. 12.5% of type 1 participants therefore had an LDL-cholesterol < 0.80 g/l versus 47.5% with normal values, the median was 1.24 g/l. 62.5% of men with T1D had lower than normal HDL-cholesterol levels, while women had low HDL-cholesterol levels were 9, 31.25%. The minimum HDL-cholesterol level was 0.1 g/l, and the maximum was 1.97 g/l, with a median of 0.53 g/l (Fig. 2).



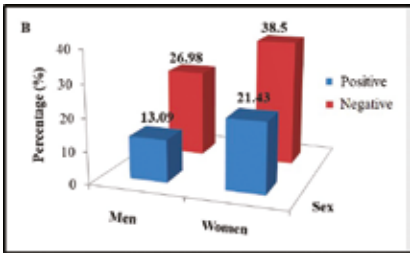
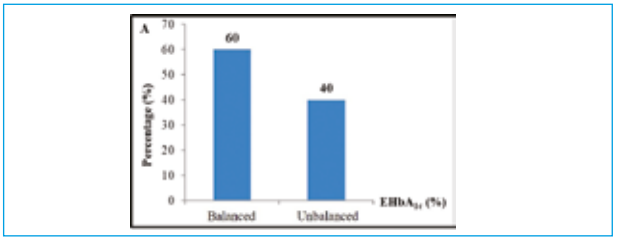
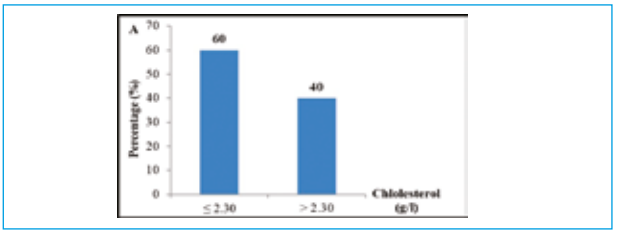
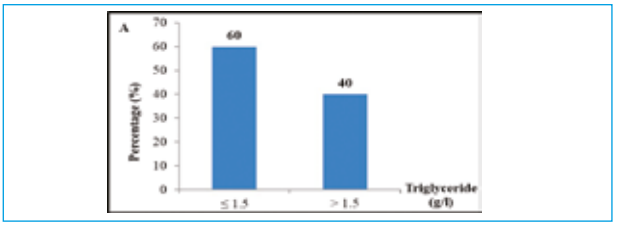


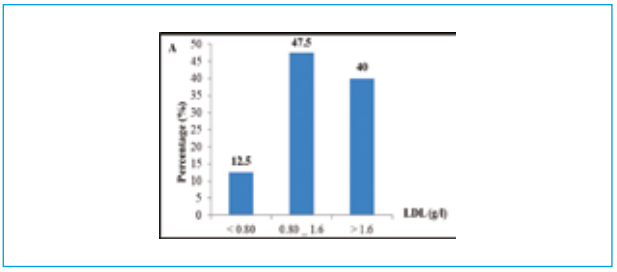
Fig. 1: (**A**) Prevalence of microalbuminuria and its distribution according to sex for T1D, (**B**) Prevalence of microalbuminuria and its distribution according to sex for T2D.

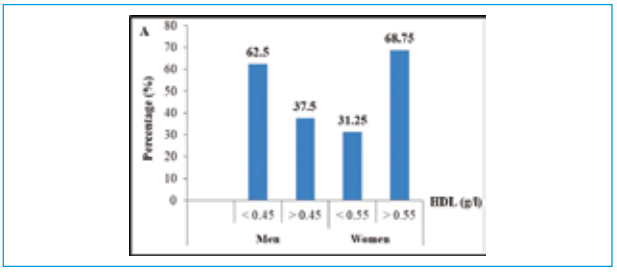
Out of all T2D, 34.52% had microalbuminuria which was absent in 65.48% of subjects (Fig. 1). The majority of T2D participants, i.e. 53.96% were unbalanced diabetics with a median of 6.7%. 78.57% of subjects with T2D had normal cholesterolemia, with a median of 1.87 g/l. 65.08% of type 2 participants had normal triglyceride levels and the median was 1.28 g/l. 55.56% of type 2 participants had normal LDL-cholesterol levels between 0.81–1.60 g/l, versus 19.84% of subjects had values higher than normal, the median was 1.07 g/l, the range was 0.14 g/l to 4.62g/l. In general, HDL-cholesterol levels were normal in 73.51% of men with T2D. In women, 55.44% had lowered values. For a minimum of 0.1 g/l and a maximum of 2.6 g/l, the median was 0.43 g/l (Fig. 2).











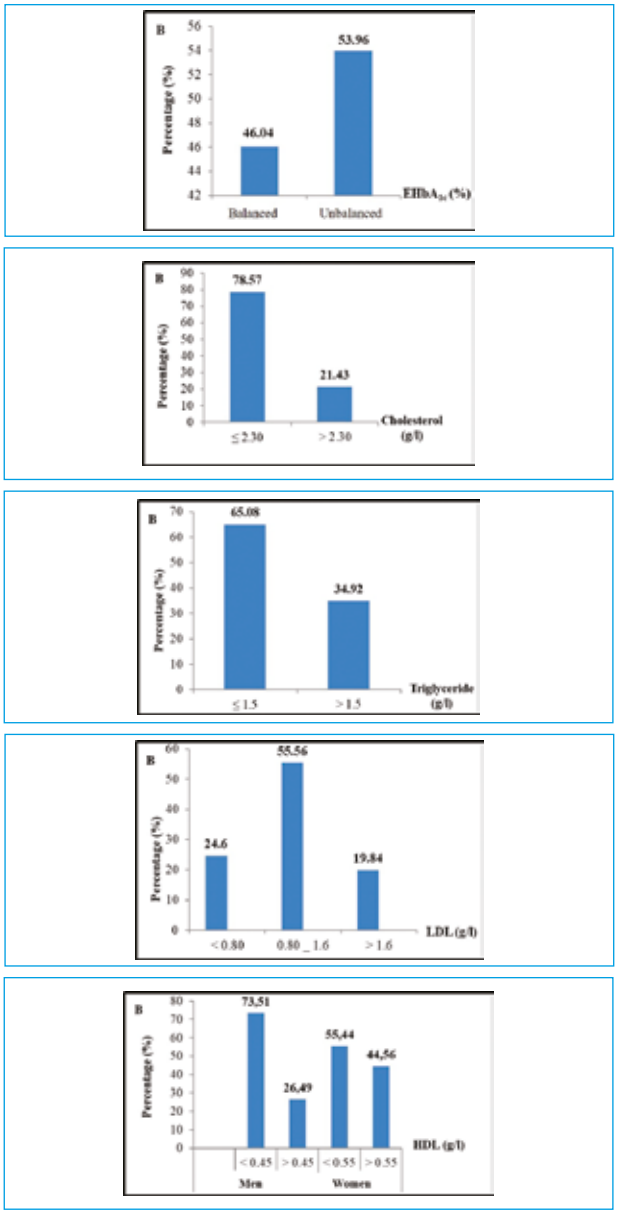


Fig. 2: (**A**) Distribution of type 1 diabetics according to glycemic and lipid levels, (**B**) Distribution of type 2 diabetics according to glycemic and lipid levels.

Risk factor for DN using bivariate analyses

Among microalbuminuric type 1 diabetic participants, a significant positive correlation ($p < 0.0001$) was found between microalbuminuria and the following parameters: SBP, DBP, EHbA1c, cholesterol, triglyceride and LDL-cholesterol (Table 2).

The X^2 test showed very strong correlations between microvascular complications (OR=8.360, 95% CI (1.970–35.462) and $p = 0.002$), alcohol consumption (OR=9.016, 95% CI (1.936-40.002) and $p = 0.0001$) and smoking (OR=9.420, 95% CI (1.987-40.523) and $p = 0.0001$) and microalbuminuria (Table 3).

Microalbuminuria in T2D showed strong correlations ($p \leq 0.00001$) with the following: abdominal perimeter, SBP, DBP, EHbA1c, cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol and ($p = 0.005$) with BMI (Table 2).

	T1D		T2D			
	Pearson's correlation		Pearson's correlation		Logistic regression analyses	
Factor	**R**	**p value**	**R**	**p value**	**Coefficient b**	**p value**
Age	0.141	0.397	0.00	0.587	-1.023	0.954
Diabetes duration	0.141	0.415	0.00	0.823	-0.658	0.364
BMI	0.245	0.138	0.173	**0.005***	-0.405	0.773
Abdominal perimeter	0.100	0.555	0.360	**0.00001***	-1.094	0.508
SBP	0.794	**0.00001***	0.714	**0.00001***	-0.043	**0.0004***
DBP	0.529	**0.0004***	0.656	**0.00001***	-3.038	0.254
EHbA$_{1c}$	0.510	**0.0007***	0.520	**0.00001***	-0.235	**0.025***
Cholesterol	0.762	**0.00001***	0.265	**0.00001***	-0.468	0.792
Triglycerides	0.728	**0.00001***	0.436	**0.00001***	-0.5887	0.644
HDL- cholesterol	0.173	0.307	0.400	**0.00001***	-1.525	**0.031***
LDL- cholesterol	0.800	**0.00001***	0.412	**0.00001***	-0.544	0.247

Table 2: Pearson correlations and logistic regression analysis.
**p = statistically significant at < 0.05.*

Correlations between microalbuminuria were significant for microvascular complications (OR=2.519, 95% CI (1.502- 4.226) and $p = 0.0004$), HBP (OR=2.930, 95% CI (9.345– 43.184) and $p = 0.00001$), alcohol consumption (OR=2.369, 95% CI (1.260-4.167) and $p = 0.0001$) and smoking (OR=2.128, 95% CI (1.300-4.101) and $p = 0.0001$), (Table 3).

	T1D				T2D			
Factor	**X^{2}test**	**p value**	**OR**	**CI (95 %)**	**X^{2}test**	**p value**	**OR**	**CI (95 %)**
HBP	$X^2 = 2.222$	0.136	8.014	**1.941–33.569**	$X^2 = 80.817$	**0.00001***	2.930	**9.345– 43.184**
Microvascular complications	$X^2 = 9.184$	**0.002***	8.360	**1.970–35.462**	$X^2 = 12.509$	**0.0004***	2.519	**1.502– 4.226**
Smoking	$X^2 = 4.904$	**0.0001***	9.420	**1.987–40.523**	$X^2 = 33.253$	**0.0001***	2.128	**1.300–4.101**
Alcohol consumption	$X^2 = 5.369$	**0.0001***	9.016	**1.936–40.002**	$X^2 = 24.621$	**0.0001***	2.369	**1.260–4.167**

Table 3: X^2 test for T1D and T2D.
*OR: Odds ratio. CI: Confidence interval. *p = statistically significant at < 0.05.*

Risk factors for DN using multivariate analyses (multiple logistic regression)

Multiple logistic regression showed that several variables were correlated with microalbuminuria, i.e., glycemic balance, SBP, and HDL-cholesterol. In contrast, BMI, cholesterol, abdominal perimeter, DBP, triglycerides, and LDL-cholesterol showed positive relationships with microalbuminuria, but none were not statistically significant (Table 2).

Discussion

Globally, the prevalence of end-stage renal disease is increasing, with DN cited as the main cause[6,9]. Epidemiological data from several countries have shown significant increases in diabetics on dialysis: i.e. 54% in the United States and Malaysia, and more than 40% in Japan, Taiwan, Hong Kong, and New Zealand[13-15]. However, in some European countries, including Romania, Norway, Scotland, the Netherlands and the United Kingdom, this rate is below 20%[16]. The aim of our study was to define microalbuminuria frequencies in

a Constantinoise population and establish possible causal links between this condition and different risk factors, based on data from the literature. Of 292 participants, type 1 diabetics accounted for 40 (13.70%) individuals, and type 2 diabetics accounted for 252 (86.30%) individuals. These frequencies were consistent with international datasets, where T2D is the most frequently encountered diabetic pathology (17-19). Women were strongly represented, accounting for 59.94% of the population, whereas 40.06% were men. This observation agrees with data from several other studies[20,21].

T2D is more common in the elderly, unlike T1D where 67.5% of the diabetics studied were under 30 years of age. These results are consistent with the literature, suggesting that T1D most often occurs before the age of 30 years, with a peak frequency at puberty[22], unlike T2D, which is diagnosed after 40 years[23]. The average patient age was 55±15.9 years, which were comparable to Tunisian patients; 49.6±9.7 years[24], Zairean patients; 48±1.8 years[25], Cote-d'Ivoirean patients; 53 years[26], Burkina Faso patients; 47±15 years[27]. The mean diabetes duration was longer in patients with positive microalbuminuria; 8.388 years versus 2.259 years in patients with negative microalbuminuria. This result was similar to other studies[28,29], suggesting a higher risk of developing microalbuminuria in patients with a long diabetic history.

In our type 1 diabetics, differences in BMI and abdominal perimeter between positive and negative microalbuminuria groups were not significant. Data from other studies contrast with our data, showing that abdominal obesity (measured by waist circumference) was an independent risk factor for microalbuminuria in type 1 and 2 diabetics[30-32]. The distribution of microalbuminurics according to BMI in type 2 diabetics showed that > 70 % had a BMI > 25 kg/m^2, with a much higher prevalence in women who presented with positive microalbuminuria. 151 patients also suffered from abdominal obesity (59.92%) (predominantly female). Similarly, other studies have suggested that abdominal obesity is associated with microalbuminuria development in type 2 diabetics[4,6,9].

Microalbuminuria was present in subjects with other microvascular complications; bivariate analysis had confirmed the presence of a significant association between microalbuminuria and retinopathy and/or neuropathy. Several studies, especially in individuals with type 1 diabetes, have demonstrated the negative effects of smoking on kidney function. For example, smokers secrete higher albumin levels than non-smokers, leading to microalbuminuria and an increased risk of cardiovascular disease[31-35]). Recent studies have provided evidence for functional and structural changes in the glomerulus, which filters blood to produce urine[1,7]. This may explain increased rates of microalbuminuria in diabetic smokers when compared to non-smokers[36].

In individuals with T1D, hypertension is usually caused by an underlying DN. The condition usually becomes evident when microalbuminuria develops. Equally, hypertension is already present at diagnosis in one third of people with T2D. Hypertension can be linked to various etiologies, including metabolic syndrome and underlying kidney damage. Hypertension ordinarily coincides with, or induces secondary causes such as the narrowing of arteries that carry blood to the kidneys[37,38]. Regardless of the underlying cause, high BP greatly accelerates DN progression[39]).

We showed that EHbA1c levels in diabetic patients (type 1 or type 2) with microalbuminuria, were significantly higher than diabetic normoalbuminuric patients, this agreed with data from several studies[34]. Long-term diabetic complications (especially T2D) can be prevented or significantly reduced by strict blood sugar control. Most adults with diabetes should aim for an EHbA1c level of 7% or lower[7].

We also showed that participants with impaired renal function had significantly increased total cholesterol ($p = 0.00001$), triglycerides ($p = 0.00001$) and LDL-cholesterol ($p = 0.00001$), but had lowered HDL-cholesterol levels when compared with subjects without microalbuminuria ($p = 0.307$). This data reflected a significant relationship of these factors with microalbuminuria. HDL-cholesterol in contrast, did not show any significant differences. In the Steno study, subjects who developed microalbuminuria had higher cholesterol levels than normoalbuminuric subjects[40]. Data from the Nephropathy Family Study (NFS) showed that average concentrations of total cholesterol and LDL-cholesterol were higher in subjects who developed microalbuminuria when compared to subjects with normal microalbuminuria[39].

A German study demonstrated predictive values for LDL-cholesterol and triglyceride cholesterol levels upon the development of persistent microalbuminuria[28]. In this study, multiple logistic regression analyses showed that several variables were related to microalbuminuria.

Glycemic balance, SBP, and HDL-cholesterol were factors strongly correlated with microalbuminuria. Triglyceride levels, total cholesterol, microvascular complications, BMI, smoking and abdominal obesity all reported positive relationships with microalbuminuria, but were not statistically significant in their associations.

Conclusions

DN is a silent killer with disastrous consequences. It was more strongly linked to glycemic imbalance and disturbances in the lipid profile. When diabetics are treated late in life, this increases the risk of kidney damage, which may be irreversible. The ideal after this work would be to continue following the same population studied for the coming years, with the establishment of strict glycemic, lipid and blood pressure control with all that that implies: diet, anti-diabetic treatments, lipid-lowering, antihypertensives and nephroprotectors ; and thus see the progression of renal involvement in microalbuminuric subjects: if there is worsening, stabilization or regression of microalbuminuria when it is reversible. See if the subjects who have shown negative microalbuminuria remain at the same stage or develop micro or even macroalbuminuria. Hence, there is a need for cooperation between treating physicians and nephrologists to reduce diabetes incidences and improve the daily lives of chronic patients. Good care and early detection are key elements in this fight.

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