ORIGINAL ARTICLE

The association between glycaemic level and lipid profile with Albuminuria in Iraqi type 2 diabetes patients — A cross sectional study

Ali Abdulateef Hassan Al-Bayati, Shatha Mohammad Jawad AL-Khateeb

Abstract

Objective: To assess the risk factors associated with diabetes on parameters of diabetic nephropathy represented by albuminuria level.

Methods: The case-control cross-sectional study was conducted at the National Diabetes Centre for Treatment and Research, Al-Mustansiriyah University, Baghdad, Iraq, from October 2019 to March 2020, and comprised adult diabetes patients of either gender who were divide into 3 groups depending on urine albumin/creatinine ratio as normal albuminuria group A, microalbuminuria group B and macroalbuminuria group C. Besides, healthy subjects were enrolled in control group D. Urine albumin/creatinine ratio was tested using urinary test strips, while glycated haemoglobin, fasting blood glucose, blood urea, serum creatinine, serum uric acid, total cholesterol, total triglycerides, high-density lipoprotein and low-density lipoprotein were tested in the laboratory. Body mass index of each subject was also measured. Data was analysed using Graph Pad Prism 8.0.2.

Results: Of the 133 subjects, 100(75.2%) were diabetes patients and 33(24.8%) were controls. Among the cases, 60(60%) were in group A with a mean age of 61.27±7.64 years; 37(61.7%) females and 23(38.3%) males; 21(21%) were in group B with a mean age of 59.48±7.63 years; 8(38%) females and 13(62%) males; and 19(19%) were in group C with a mean age of 62.79±9.73 years; 7(37%) females and 12(63%) males. Among the controls in groups D, there were 20(%) females and 13(%) males with an overall mean age of 54.36±10.94 years. Among the cases, 40(40%) had some degree of diabetic nephropathy. Glycated haemoglobin and fasting blood glucose were significantly higher among the cases and were strongly positively correlated with albuminuria microalbuminuria and macroalbuminuria ($p<0.01$). Total cholesterol and low-density lipoprotein were positively correlated with macroalbuminuria, while high-density lipoprotein was negatively correlated with albumin/creatinine ratio in microalbuminuria and macroalbuminuria ($p<0.05$).

Conclusions: Diabetic subjects with nephropathy usually had poor glycaemic control with dyslipidaemia.

Keywords: Diabetic nephropathy, Albuminuria, Glycaemia, Dyslipidaemia. (JPMA 71: S-57 [Suppl. 8]; 2021)

Introduction

Diabetes mellitus (DM) is a chronic metabolic illness associated with severe or even life-threatening complications. DM prevalence represents a global challenge, as in 2019 the total number of diabetics reached 463 million, and the number is expected to continuously and rapidly expand to reach up to 700 million in 2045.[1] This spike in prevalence globally is associated with increasing mortality and morbidity related to diabetic complications.[2]

Diabetic nephropathy (DN) is one of the commonest complications of DM and is regarded as the leading cause of end-stage renal disease (ESRD).[3] An early sign of DN would be microalbuminuria, which can be measured as concentration of albumin in 24-hour urine, and expressed as a ratio of urinary albumin to creatinine (A/C ratio).[4] The pathophysiology of DN is complicated due to the dysfunction of the glomerular basement membrane that facilitates the excretion of albumin in urine. The amount of urinary albumin is considered normal with albumin in urine <30mg per day. Values between 30mg and 300 mg per day represent microalbuminuria and >300mg per day indicates macroalbuminuria.[5] The importance of early detection of microalbuminuria is vital as in this stage the deterioration of DN can be stopped or even reversed by achieving good glycaemic management.

Diabetic patients suffer from several metabolic abnormalities that collectively result in progressive inflammation and tissue damage. Factors, such as increased intracellular glucose, glycation of proteins, hexosamine pathway, oxidative stress (OS) and others have been implicated.[6] Hyperglycaemia per se can cause microangiopathy and thickening of the capillary basement membrane due to a direct reaction with the arterial wall to form glycation of wall protein that leads to the thickening of the capillary basement membrane and increased vascular

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permeability.[7] The severity and duration of hyperglycaemia are detrimental factors of DN. Studies showed a strong correlation between bad glycaemic control and progression of renal disease and deterioration of kidney functions.[8,9] Furthermore, data from a large trial showed that good glycaemic control could reduce and even prevent the transition of microalbuminuria to ESRD.[10]

Dyslipidaemia is a metabolic abnormality usually associated with diabetes. It has been reported that diabetic patients showed raised triglycerides (TG), low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) levels, and decreased high-density lipoprotein (HDL).[11] In DN, variable lipid abnormality has been reported. Reduced insulin action in DN patients is associated with reduced level of good cholesterol HDL.[11] A study showed that a high serum level of TG, low-density lipoprotein (LDL and total cholesterol (TC) are associated with albuminuria.[12] In Iraq, a study conducted in 2013 by Ali and Al Lami,[13] showed no significant association between lipid profile abnormalities with microalbuminuria in DN patients. Hasan and Al-Rubaei[14] in 2017 showed high serum level of TG, LDL and TC, and low HDL in DN patients with DN.

The current study was planned to analyse the various factors in addition to the effects of glycaemia on the parameters of DN.

Subjects and Methods

The case-control cross-sectional study was conducted at the National Diabetes Centre for Treatment and Research, Al-Mustansiriyah University, Baghdad, Iraq, from October 2019 to March 2020. After approval from the institutional ethics review committee, the sample size was calculated using Open epi sample size calculator[15] based on 90% power to detect an effect of 10%, with a significance level of 0.05 and confidence level of 95%.

The sample included adult diabetes patients of either gender who were divided into 3 groups depending on urine A/C ratio as normal albuminuria group A, microalbuminuria group B and macroalbuminuria group C. Besides, healthy subjects were enrolled in control group D.

After taking verbal consent, venous blood and urine samples were taken from all the participants. Urine samples were used to measure albuminuria with a special microalbumin auto analyser (Combilyzer-13, Human Company, Germany). HbA1c was measured using anti-coagulated whole blood (SD A1cCareTM system, Biosensor, South Korea). Biochemical tests included fasting blood glucose (FBG), blood urea, serum creatinine, serum uric acid, TC, TG, HDL and LDL (Biolabo, France). Body mass index (BMI) was calculated with the standard method of BMI = weight (Kg) / square height (m^2).

Data was analysed using Graph Pad Prism 8.0.2 (263). Data was expressed as mean ± standard deviation. The significance of difference was tested using students t test. Pearson correlation was calculated for the correlation between two quantitative variables with its t-test for testing the significance of correlation. The correlation coefficient value (r) was either positive having direct correlation, or negative having inverse correlation. Statistical significance was considered at $p<0.05$.

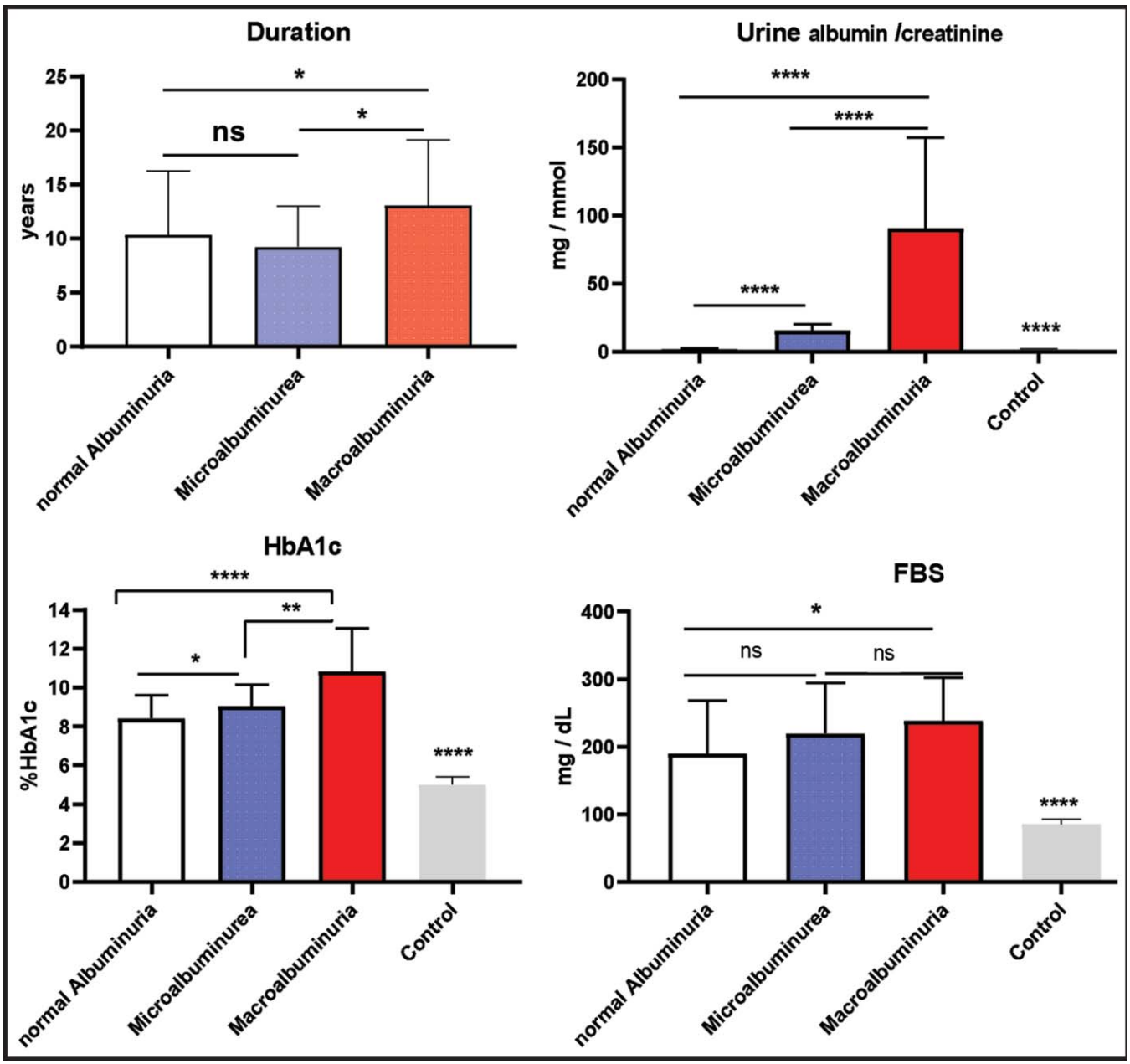
Results

Of the 133 subjects, 100(75.2%) were diabetes patients

Table-1: Anthropometric and biochemical characteristics of the subjects.

Variables	Control N=33	Diabetic with normal albuminuria N=60	Diabetic with Microalbuminuria N=21	Diabetic with Macroalbuminuria N=19
Age years mean±SD	54.36±10.94	61.27±7.64	59.48±7.63	62.79±9.739
Sex F/M	20/13	37/23	8/13	7/12
BMI Kg/m^2 mean±SD	27.76±2.55	29.93±5.08	30.62±3.13	30.48±5.04
Duration years mean±SD	---	10.33±5.94	9.24±3.78	13.05±6.1
FBG mg/dl mean±SD	85.36±7.65	189.7±78.35	219.4±74.60	238.6±63.96
HbA1C % mean±SD	5.05±0.40	8.43±1.17	9.03±1.13	10.83±2.22
Blood Urea mg/dl mean±SD	27.85±5.63	37.77±20.05	37.95±21.44	48.59±29.15
Creatinine mg/dl mean±SD	0.6±0.13	0.80±0.34	0.87±0.467	1.03±0.42
Uric Acid mg/dl mean±SD	4.17±1.0	4.770±1.467	4.51±1.26	4.94±1.45
Urinary (A/C) Ratio mg/mmol	1.75±0.58	1.825±0.53	15.53±4.767	90.63±66.58
Cholesterol mg/dl mean±SD	186.7±42.09	184.7±54.70	212.6±36.39	221.6±34.20
TG mg/dl mean±SD	140.6±74.33	198.2±67.38	218.1±68.66	216.7±70.18
HDL mg/dl mean±SD	45.97±18.09	34.62±10.69	28.57±9.94	22.68±9.23
LDL mg/dl mean±SD	88.82±39.24	109.8±52.74	121.3±52.74	143.9±35.81

SD: Standard deviation, F: Female, M: Male, BMI: Body mass index, FBG: Fasting blood glucose, HbA1c: Glycated haemoglobin, A/C: Albumin/creatinine, TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.



NS: Non-significant differences, * P. value <0.05, ** P. value <0.01, **** P. value <0.0001.

Figure: Duration of type 2 diabetes, urinary albumin/creatinine (A/C) ratio, fasting blood glucose (FBG) and glycated haemoglobin (HbA1c).

and 33(24.8%) were controls. Among the cases, 60(60%) were in group A with a mean age of 61.27±7.64 years; 37(61.7%) females and 23(38.3%) males; 21(21%) were in group B with a mean age of 59.48±7.63 years; 8(38%) females and 13(62%) males; and 19(19%) were in group C with a mean age of 62.79±9.73 years; 7(37%) females and 12(63%) males. Among the controls in groups D, there were 20(%) females and 13(%) males with an overall mean age of 54.36±10.94 years (Table-1).

Among the cases, 40(40%) had some degree of diabetic nephropathy. HbA1c and FBG were significantly higher among the cases and were strongly positively correlated with microalbuminuria and macroalbuminuria (p<0.01). TC and LDL were positively correlated with macroalbuminuria, while HDL was negatively correlated with A/C ratio in microalbuminuria and macroalbuminuria (p<0.05) (Table-2).

Duration of type 2 DM (T2DM), urinary A/C ratio, FBG and HbA1c were also analysed and compared among the

Table-2: Correlational statistics of urinary albumin/creatinine ratio with other variables.

Variables	Control N=33	Diabetes with normal albuminuria N=60	Diabetes with Microalbuminuria N=21	Diabetes with Macroalbuminuria N=19
Age	0.279	0.327	0.582	0.52
P. value	0.058	0.005	0.003	0.011
BMI	0.198	-0.103	0.589	0.643
	0.135	0.216	0.002	0.002
Duration	---	-0.056	-0.186	0.066
		0.336	0.209	0.394
FBG	0.121	0.038	0.446	0.591
	0.232	0.387	0.021	0.004
HbA1C	0.176	0.023	0.552	0.547
	0.164	0.432	0.005	0.008
Blood Urea	0.337	-0.061	0.351	-0.065
	0.027	0.321	0.06	0.395
Creatinine	0.293	-0.041	0.072	-0.099
	0.084	0.378	0.378	0.343
Uric Acid	0.135	-0.109	-0.07	-0.158
	0.016	0.204	0.382	0.259
Cholesterol	0.212	0.119	0.179	0.465
	0.911	0.183	0.218	0.022
TG	0.138	0.134	-0.319	-0.067
	0.222	0.154	0.079	0.392
HDL	0.18	0.032	-0.389	-0.638
	0.159	0.403	0.041	0.002
LDL	0.314	0.089	0.134	0.421
	0.083	0.25	0.261	0.036

BMI: Body mass index, FBG: Fasting blood glucose, HbA1c: Glycated haemoglobin, TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

groups (Figure).

Discussion

A large number of diabetic patients suffer from DN which represents a leading cause of ESRD. In this study, 40% of T2DM patients had some degree of DN; 21% had microalbuminuria and 19% had macroalbuminuria, as detected by elevated urinary C/A ratio. These results are in line with earlier results, Rao.[16] There was a male preponderance among those having DN which is consistent with studies.[17]

In T2DM patients, the occurrence of albuminuria increases with age, with elderly diabetic individuals at increased risk for ESRD.[18] The results of the current study showed that there was no difference in mean age in the three T2DM groups. However, correlation analysis showed strong association of increasing albuminuria with age within the groups (Table-2).

The duration of diabetes is usually associated with the development of a chronic complication. In this study, patients with macroalbuminuria had significantly higher duration than those of the other groups. No correlation was observed in all the study groups. These results are similar to earlier ones, Song, Jeong.[19]

In the current study, there was a significant association between BMI and albuminuria. a study found that BMI was one of the factors positively related to renal dysfunction.[19]

It is well known now that achieving good glycaemic control for T2DM patients can prevent or even reverse the complications associated with diabetes. Regarding the degree of glycaemia, the current study showed that the mean FBG was significantly higher in diabetic groups than in the control group. Regarding the degree of glycaemia, only significant difference in mean FBG were observed within the diabetic groups. Correlation analysis revealed that both microalbuminuria and macroalbuminuria were associated with increasing albuminuria. This finding was also in line with literature Kundu, Roy.[20] In the current study, mean HbA1c level was significantly different between the diabetics and the controls, and within the diabetes groups, significant difference was observed between normal albuminuria and microalbuminuria, highly significant differences were observed between macroalbuminuria and both normal albuminuria and microalbuminuria. Furthermore,

a highly significant association between level of HbA1c and albuminuria was observed in both microalbuminuria and macroalbuminuria, while no such association was observed in normal albuminuria and control groups. These results are consistent with other researches in Iraq[21] and other countries.[20]

Long duration of abnormally high glucose and lipid disarrangements are regarded as root causes for diabetic complications, including DN.[22] The recorded lipid abnormalities that seem to be associated with increased risks of albuminuria are high levels of TC, TG and LDL, with consistently low HDL.[12]

Regarding TC, there were significant differences in mean values between microalbuminuria and normal albuminuria groups ($p<0.05$). In addition, a highly significant difference was observed between macroalbuminuria and normal albuminuria group ($p<0.01$), but no significant difference in the mean values of macroalbuminuria and microalbuminuria groups ($p=0.426$). Correlation analysis revealed an association between high cholesterol and albuminuria in only the macroalbuminuria group. These findings are consistent with the findings of the above studies.[12,22]

No significant difference was observed in mean TG values between microalbuminuria and normal albuminuria groups, but TG significantly increased in the macroalbuminuria compared to normal albuminuria group. Correlation analysis showed no association of changes in TG level with increasing urinary A/C ratio in the study groups. Correlation analysis showed findings different from what has been reported earlier by Tien, Tu.[23] This variability could be attributed to small sample size in the current study.

A significant high level of LDL in macroalbuminuria was noted compared to microalbuminuria and normal albuminuria groups. No difference was observed between microalbuminuria and normal albuminuria groups. Correlation analysis showed a positive association between increasing LDL level and the increasing urinary A/C ratio in only macroalbuminuria group, and no such associations were noted in any other group. These results seem to be comparable with previous studies[22,24] except the correlation of LDL with microalbuminuria, which can be attributed to sample size and low statistical power for mild increases.

HDL analysis of the current study was consistent with previous researches.[12,23]

Conclusions

T2DM is a long-lasting disease which is complicated by DN. Different variables had effect on or correlation with the degree of albuminuria. Early detection of microalbuminuria might decrease the risk of progression of renal problem by adequate diabetes management.

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