



Early Proteinuria in Adult Algerian-Onset Diabetes

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ABSTRACT

Diabetes mellitus is a common endocrine disorder chronic metabolic affecting the metabolism of carbohydrates, lipids, proteins and enzyme activities. Diabetes mellitus is a disease not without complications, including acute metabolic complications and chronic complications that are the basis of a very high mortality rate. The subject of this study consists of 43 diabetics (adult-onset), 10 possible prediabetics and 20 normal subjects. Total proteins and electrophoretic pattern are estimated both in urine and plasma. Total urinary protein output is higher in diabetics than normal. The more the duration of the disease, the greater is the amount of protein lost in urine. This proteinuria is non-global and only three fractions appear in urine, Albumine – Globuline ($\alpha_1 + \alpha_2$). Correlation between the degree of proteinuria and the blood glucose level as well as the amino acid nitrogen lost in urine is recorded. Also correlation between proteinuria in these patients and creatinine clearance and blood urea is shown. In the prediabetics only four patients had increased total protein out put than normal. We conclude that there is a slight degree of impairment of kidney function as well as some disturbance in protein metabolism in the investigated cases.

Keywords: Amino acid nitrogen, Creatinine, Diabetes, Proteinuria, Nephropathy,

INTRODUCTION

Diabetes mellitus is a common endocrine disorder chronic metabolic affecting the metabolism of carbohydrates, lipids, proteins and enzyme activities. Diabetes mellitus is a disease not without complications, including acute metabolic complications and chronic complications that are the basis of a very high mortality rate.

Diabetic nephropathy accounts for 6% of deaths among diabetics.^{1,2} Early in the course of the disease, even in the prediabetic state, there is increased thickening of the glomerular capillary basement membrane.^{3,4} This alteration in the structure of the basement membrane is reflected as changes in excretion of protein.

In this work we study the amount and pattern of urinary protein out put and plasma proteins in diabetics patients with adult-onset diabetes Also we examine a number of possible prediabetics for the existence of proteinuria.

MATERIALS AND METHODS

Three groups of subjects are studied.

(A) – Diabetic group: 43 patients with adult-onset diabetes, (disease starting after the age of 35). They are 44 – 67 years old and are divided into 2 subgroups.

1. Patients who had the disease for more than 5 years (16 cases).
2. Newly diagnosed patients or those had the disease for less than 5 years duration (27 cases).

3. Possible prediabetics: 10 adults with no clinical or laboratory evidence of diabetes (using ordinary as well as provocative tests). In the case of 8 these patients, both parents, had documented diabetes. The other 2 were females with large first babies.

Control group

20 apparently healthy adults in the same age as the patients. They are 10 males and 10 females with normal oral glucose tolerance tests (GTT) and no history of diabetes in parents or near relatives.

Investigations done

Urine analysis

1. Estimation of total 24 hours urinary protein. A turbidimetric method using trichloroacetic acid as a precipitating agent on concentrated urine was used.⁵
2. Agar gel electrophoresis of urinary protein using a technique based on methods by Cowley.⁶⁻⁸
3. Creatinine clearance test.⁹

Blood analysis

1. Blood glucose level using an enzyme oxidase method (Kits)¹⁰, 2 hour post prandial levels are shown.
2. Estimation of plasma total proteins, using a Biuret method¹¹
3. Electrophoretic separation of serum proteins by cellulose acetate by Afonso¹²
4. Estimation of blood urea¹³



Table 1: Urinary total Protein and Fractional proteins (mg/day) in normal and adult-onset diabetics

		Total Protein	Albumin	Globulins				A/ $\alpha_1 + \alpha_2$
				α_1	α_2	β	γ	
Control	Mean	151	138	13.0	-	-	-	10.72
	SE \pm	10	11.2	3.5				0.77
Diabetics <5Y	Mean	206	153.9	31.8	20.3	-	-	2.9
	SE \pm	12	7.2	3.3	1.8			0.12
P ₁		< 0.01	< 0.02	< 0.01	< 0.001			< 0.001
Diabetics > 5Y	Mean	360	237	115	8.2	-	-	1.76
	SE \pm	28	10	13	6			0.25
P ₂		< 0.001	< 0.001	< 0.001	< 0.001			< 0.001

5Y = duration of disease is less than < 5Y, **5Y** = duration of disease is less more > 5Y, **P₁** = significance D. 5Y/ controls , **P₂** = significance D. 5Y/ controls

Table 2: Comparison between urinary total protein, blood glucose, urinary, A.A.N. Creatinine clearance and blood urea in Adul-onset Diabetes. (Mean \pm S.E.)

No of cases		25	15	8	5
Total proteins mg/day	Mean	300	300-400	400-500	500
	S.E \pm	5	7.5	4.3	7.8
Blood glucose mg%	Mean	217.4	251.2	307.12	337
	S.E \pm	2.2	4.5	4.8	6.6
A.A.nitrogen mg/ day	Mean	253	289	340	372
	S.E \pm	4	5	6.6	8.8
Creatinine Clearance mg/ml	Mean	89	82	73	68
	S.E \pm	0.8	0.92	1.2	1.5
Blood urea mg%	Mean	19.5	23	27	31
	S.E \pm	0.2	0.32	0.11	0.23

Table 3: Plasma proteins (Total and Fractional) in adult-onset diabetics

		Total protein mg%	Albumin	Globulins				A/G	A.A.N mg%
				α_1	α_2	β	γ		
Control	Mean	7.41	4.55	0.27	0.46	0.66	1.4	1.6	6.6
	S.E \pm	0.10	0.079	0.07	0.01	0.02	0.04	0.4	0.16
Diabetics <5Y	Mean	7.25	3.99	0.26	0.56	0.66	1.50	1.3	8.8
	S.E \pm	0.09	0.06	0.1	0.02	0.03	0.01	0.03	0.2
P ₁			< 0.01	N.S	< 0.05	N.S	N.S	< 0.2	< 0.01
Diabetics > 5Y	Mean	7.14	3.86	0.36	0.56	0.66	1.59	1.2	11.46
	S.E \pm	0.06	0.09	0.01	0.02	0.01	0.02	0.05	0.3
P ₂			< 0.01	< 0.01	< 0.05	N.S	N.S	< 0.01	< 0.001

5Y = duration of disease is less than < 5Y, **5Y** = duration of disease is more than > 5Y, **P₁** = significance D. 5Y/ controls, **P₂** = significance D. 5Y/ controls.

RESULTS

The results obtained are shown in tables (1-3) and figures (1 & 2).

DISCUSSION

In the present work, total urinary protein output is significantly higher in the diabetic group than in the control group (Table 1). This agrees with previous workers, who showed that diabetic patients excrete more proteins in their urine than normal.¹⁴⁻¹⁶ We notice

however that our figures for physiological proteinuria is higher than that reported for European normal subjects.^{14,16} But¹⁷ also found high results with his Egyptian normal controls. The duration of the disease seems to affect the degree of proteinuria.

Patients, who had diabetes for more than 5 years, have higher amounts of protein in their urine than those with less than 5 years duration (Table 1). Adult diabetics lose more albumins in their urine samples than normal. Electrophoresis of their urine samples show that the



proteinuria of our patients is selective as only (Alpha1) and (Alpha2) globulins appear with the albumin while (Beta) and (Gama) fractions are not detected. The excretion of globulins increase with the duration of the disease and the A/G ratio drops to 1.6 and then to 1.3 compared to 10.7 in the normal controls. In (Table 2) we study the relationship between the degree of proteinuria and the metabolic state of the patients.

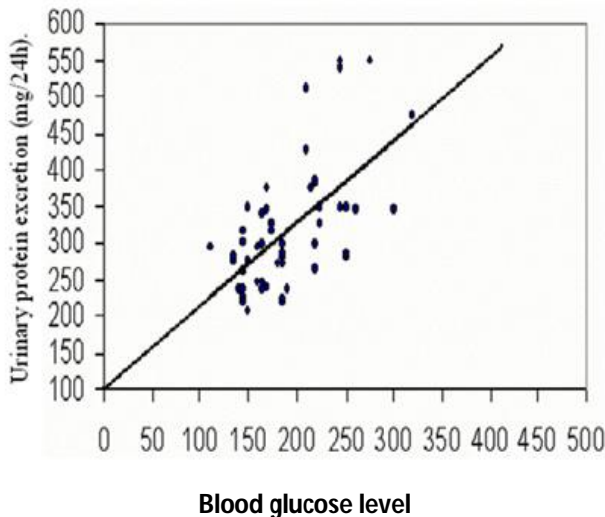


Figure 1: Blood sugar 2hr post prandial mg/100ml

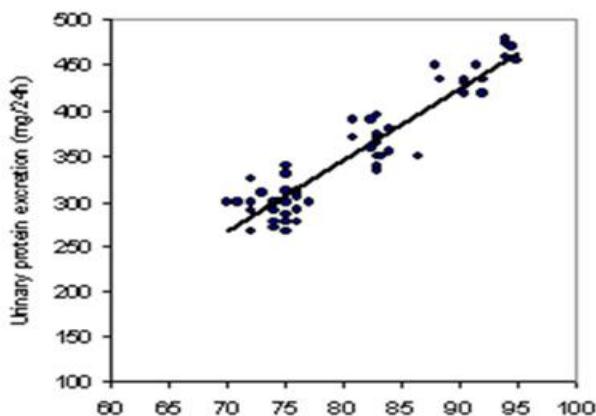


Figure 2: Creatinine clearance mg/ml.

A positive correlation is noticed with the blood glucose level, measured 2 hours postprandial and a linear relationship is shown in (Figure 1). In (Table 2), we also study the relationship between the degrees of proteinuria with other kidney function tests. We find that as the amount of protein in cases; there is progressive drop in the 24 hours creatinine clearance (Figure 2) together with a gradual rise in the blood urea level, reported¹⁸ that renal hyper-function, hypertrophy and elevated G.F.R, are characteristic findings in early diabetic states.

The kidney hyper function continues until the onset of proteinuria, upon which G.F.R starts to decrease. The above results, suggest that in maturity onset diabetes there is a certain of impairment of kidney function. This is evidenced from the less of protein (both albumin and globulins) in urine, the decrease in creatinine clearance

and the increase in blood urea , whether these changes appear early or not in the disease is a matter of controversy^{3,4,19} noticed signs of diabetic glomerulosclerosis before evidence of glucose intolerance. They stated that thickening of glomerular capillary basement membrane occurs in recently diagnosed diabetics and even in prediabetics. They suggested a genetically determined diathesis for diabetic glomerulosclerosis. On the other hand, claimed that protein excretion in prediabetics was within normal range.²⁰

In our work only four out of the ten possible prediabetics chosen, showed a small but significant elevation total protein in urine (172, 177 and 183 mg / day). The fraction elevated was albumin. In two subjects Alpha1 globulin was also detected. Hemmingsen,^{15,21,2,16} suggested the likelihood of diabetic glomerulosclerosis to increase with the duration of the disease.

This is confirmed in our work as the amount of albumin and globulins lost in urine is more in the patients who had the disease for more than 5 years, than in those with less than 5 years duration. On top of these changes in the kidney function, there seems to be also some disturbance in protein analysis (Table 3), show that our patients have a certain degree of hypoproteinuria.

This lowering of plasma proteins is mainly secondary to hypoalbuminuria. The fall in serum albumin is unlikely to be due to proteinuria alone, as most of our cases did not yet develop nephritic syndrome with massive proteinuria. Defective synthesis, inadequate caloric intake and excessive breakdown of protein may be other possible factors.

REFERENCES

1. Campbell RC, Ruggenti P, Remuzzi G, Curr.Diab.Rep., 3(6), 2003, 497.
2. Solomon P, De Wayne A, Diabetic glomerulosclerosis, Contr. Nephrol, 1977, 7.
3. George F, Gahill Jr, Diabetes Mellitus: In Cecil text book of Medicine by Paul, B. Mc Dermott, W. and Wyngaarden, J .ed. W.B. Saunders Co Philadelphia, London, 1979.
4. Daysog A, Dobson HL, Prennan JB, "Renal glomerular and vascular lesions in prediabetics", Ann. Int. Med., 54, 1961, 672.
5. Ditzel J, Junker K, Abnormal glomerular filtration rate, renal protein excretion in recent and short term diabetics, British Med., J.2, 1971, 13-19.
6. Cawly L.P, Electrophoresis and Immunoelectrophoresis, Churchill Livingstone-Edinburgh and London, 1969.
7. El Hawary MF, Simple cells for gel and immuno electrophoresis J of Egyptian Medical Assoc, 51, 1969, 9.
8. Graber P, Burtin P, Immuno-electrophoretic analysis, Elsierv publishing company, 1964.

9. Valery H, Creatinine clearance test. In practical biochemistry by Harold Varly 4th ed, William Heinemann – medical books London, 1969, 175.
10. Werner WC, Rey G, Wie linger H, Test combination glucose z. analyt. Chem., 252, 1970, 224.
11. Gornall AG, Bardwill CJ, David MM, Determination of plasma proteins, J.Biol. Chem., 177, 1949, 75.
12. Afonso E, The electrophoresis of proteins on cellulose acetate membranes, Clin. Chim. Acta., 6, 1961, 883-885.
13. Vaalery H, Determination of blood urea in practical clinical biochemistry by Harold Varley 4th ed. William Heinemann medical books London, 1979, 171.
14. Teitz N, Quantitative test for urinary proteins in fundamental of clinical chemistry Ed. Norbet Teitz second edition, Saunders comp, 1969, 360.
15. Hemmingsen L, Hoiby N, Kragh-Sorensen P, Protein and LDH, Isoenzyme pattern of the urine from patients with diabetes mellitus – Diabetologia, 6, 5., 12, 1970, 518.
16. Virella LM, Virella G, Rosenbrook J, Gonzalez J, Colwell J, Early diagnoses of renal mal function in diabetics – Diabetologia, 16, 1979, 165-171.
17. Zahran MM, Fayek W, Serum and urine proteins in calcular non-bilharzial patients, Egyptian J. of urplogy, IV, 2, 1978.
18. Mogensen CE, Progression of nephropathy in long-tern diabetics with proteinuria and effect of initial antihypertensive treatment, Sccond. J. Clic. Lab Invest., 36, 1975, 83-38.
19. Nash DA, Rogers FW, Langlianais PG, Bunn S, Diabetic glomerulo sclerosis without glucose intolerance, Am. J. Med., 59, 1975, 191-199.
20. Balodimos MC, Diabetic nephropathy in “Diabetes Mellitus “ 11th ed . by Marble A , White, P and Bradly R.F. Lea, Febiger Philadelphia, 1971.
21. Miki E, Kuzuya T, Nakao K, Frequency, Degree and Progression with time of proteinuria in diabetic patients Lancet, i-4, 2, 1972.

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