Evaluation Of Microalbuminuria As A Marker Of Nephropathy In Type 1 Diabetic Children In Mosul

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Abstract

Diabetic nephropathy (DN) is proved to be the most common cause of death in type 1 diabetics and Microalbuminuria MA is the only sign in the reversable stage of diabetes nephropathy

The aim of the present work is to evaluate the presence of MA as a screening test in type 1 diabetic children and to study the relation between MA, duration and severity in a case control study. Seventy two patients with type 1 DM was enrolled with twenty four apparently healthy child as a control group. Urine MA, urine creatinine, fasting plasma glucose, Glycosylated hemoglobin (HbA1c), serum urea and creatinine were measured in both groups. MA was evaluated using morning spot sample and it was determined using urine albumin / creatinine ratio. Statistical analysing including Z-test , X^2, linear regression analysis revealed a positive correlation between urine albumine creatinine ratio (UACR), severity and duration of DM. According to the 95% percentile confidence limit (mean$\pm$2SD) of the control groups, the cut off value was determined and accordingly 36.1% of the patients studied proved to have positive MA.

In conclusion the duration, severity of DM play an important role in decreasing the possibility of DN, Regular measurement of MA (with highest priority to HbA1c as a glycemic index), MA should decline substantially which should in turn lower the number in whom overt proteinuria and end-stage renal disease developed.

الخلاصـــــة

يعتبر اعتلال الكلية الناجم عن داء السكري هو أحد الأسباب الشائعة للوفيات في داء السـكري النـوع الأول، وأن الـزلال الميكروسكوبي البولي هو العلامة الوحيدة والمبكرة لاكتشاف الاعتلال الكليوي في مرضى داء السكري القابلة للعلاج.

أجري البحث لتقييم وجود الزلال الميكروسكوبي البولي كفحص تحري في الأطفال المصـابين بـداء السـكري نـوع (1) ودراسة العلاقة بينها وبين فترة وشدة مرض السكري لديهم. نفذت الدراسة في مختبر تخصصي في الكيمياء السريرية خاص بأحـد الباحثين للفترة من من أيار 2002–كانون الأول 2003. شملت الدراسة اثنا وسبعون من الأطفال المصابين بداء السـكري نـوع 1 وأربع وعشرون من الأطفال الأصحاء (عينة سيطرة). تم جمع المعلومات السريرية: العمر، الجنس، الفترة الزمنية وشـدة مـرض السكري. تم قياس تركيز الزلال الميكروسكوبي البولي، الكرياتينين في البول اليوريا والكرياتينين في مصل الدم، الكلوكوز في حالة الصيام في مصل الدم، إضافة إلى الهيموكلوبين السكري نوع (HbA1c) واستخراج نسبة الألبومين/الكرياتينين فـي البـول فـي الأشخاص المذكورين أعلاه، تم تحليل التباين باستخدام فحص(Z) لمتوسطين ومربع كـاي (X^2)، معادلـة الإنحـدار، التحليـل الإنحداري المتعدد لتقدير التأثيرات الأيضية المتغيرة على الزلال البولي الميكروسكوبي والسيطرة السكرية. أظهرت النتائج إيجابيـة الزلال الميكروسكوبي البولي في 36% من المرضى السكريين نمط 1/ كما ولوحظ وجود علاقـة مهمـة بـين نسـبة الـزلال-الكريايتنين في البول وشده وفترة الإصابة بالسكري (معامل الارتباط البسيط =0.7، ب=0.001).

Introduction

Diabetic nephropathy is supposed to develop in about 30% of patients with type 1 diabetic mellitus (DM)(1) , however, it varies between 5-22% (2).In addition, as the presence of microalbuminuria (MA) indicates incipient nephropathy, it may precede and predict overt diabetic nephropathy(3).Further, diabetic nephropathy (DN) is still the main reason for end-stage renal failure, dialysis and Kidney transplantation in the western world(4).MA is defined as albumin excretion rate (AER) between 20 and 200µg/min (30-300mg/24hours)(5) and it termed persistent whenever it occurs in minimum two out of three measurement(6).MA is considered a clinically important indicator for deteriorating renal function in diabetic subjects. It is now accepted by both European and American diabetic societies that regular screening of urine albumin excretion (UAE) is valuable in monitoring both type 1 and type 2 diabetes(7).

A variety of protocols with timed urine collection have been developed to diagnose MA(8). All these protocols are impractical and the convenient alternative is the rate of concentration of urine albumin and creatinine (UACR) measured in a random voids(9,10).By using first-void morning urinary sample not only albumin concentration but albumin to creatinine ratio could be determined and it is recommended to eliminate the consequences of different concentration of urine sample observed(11).Most recently an evaluation made by using the receiver operator characteristics (ROC) curve and the albumin / creatinine ratio proved to be a more accurate indictor than albumin concentration(12).

The aim of the present work is to evaluate the presence of MA as a screening test in type 1 diabetic children, and to study the relation between MA, duration and severity of DM.

Material and Methods

This is a case-control study in which (82) randomly chosen diabetic children with type 1DM attending one of the author,s clinical chemistry laboratory (Mosul) between May2002-December 2003. They were refereed for the assessment of their glycemic control, urine for MA and/or renal function tests. Care was taken to exclude those patients with pre existing congestive cardiac failure, urinary tract infection, hypertension and all conditions likely to produce MA according to the review of their physicians.

The control group includes (24) apparently healthy child (18 males and 6 females). The mean ±SD of (8.79±4.25), age range of (4-12) years. They were selected during urine analysis.

Sulphosalicylic acid solution (20%) used for semiquantitative measurement of urine protein(13).Positive urine samples indicate that these patients were considered to have overt proteninuria and accordingly 10 samples were not analyzed further, those (72) patients with negative test were subjected to the real study. They were 53 males and 19 females their mean age ± SD were (7.60 ±2.29) with age range (3.5-12) years.

The glycemic control was assessed by measuring the fasting plasma glucose (FPG) immediately using the spectrophotometeric enzymetic endpoint method(13),and the glycosylated hemoglobin (HbA1C) using the ion exchange resin method. Stanbio (USA). The alkaline picrate solution was used for the spectrophotometric measurement of both serum and urine creatinine (Jaffe's reaction), Randoux (UK). Serum urea was measured by urease bertholet

spectrophotometric endpoint method, Bicon (Germany).

The first void morning samples were analyzed for MA after the proper centrifugation and the MA in the supernatant was assessed by immunoturbidemtric method reaction. In specific detection of human albumin as end point of Antigene-Antibody reaction, Randoux (UK).

The test, was repeated twice in each patient during the next visit of other check of plasma glucose at 3-4 weeks interval before being considered as positive tests.

The glycemic control was graded as good (FPG < 7.15 mmol/L and /or HbA1c < 6.8%), fair (FPG 7.15-8.25 and/or HbA1c 6.8-7.6) or poor control (FPG > 8.25 and/or HbA1c > 7.6)(14).

Results

Seventy two diabetic children were enrolled in this work. Fifty three (74%) were males and 19(26%) were females with an age range (3.5-12) years. The average duration of diabetes was (3.22±2.0) years with a range of (0.5-9) years.

MA represented in this work as UACR by using the morning spot samples. The ratio of the concentration of albumin to creatinine was used as an index of UAE. Depending on the cut off value of UACR which was determined by the 95th percentile of the distribution of UACR in the non diabetic individual (control group) (mean±2SD). 26 patients (36.1%) found to have UACR above the cut off value and considered as positive for MA.

Table (1) shows the clinical anthropometric characteristics of the studied groups.

In Table (2), amongst 8 patients with good glycemic control according to FPG 2 patients (7.7%) had MA in comparison to 22 patients having MA with poor glycemic control (P<0.001).

In Table (3), amongst the (45) patients with good glycemic control according to HbA1c%, 5 patients (19.2%) had MA in comparison to 16 patients (61.5%) having MA with poor glycemic control (P<0.001).

Figure (1) and (2) show that there is a positive correlation between UACR, duration and severity r=0.7, P<0.001.

Discussion

It is indispensable to carefully monitor all patients with type 1 DM for evidence of renal disease. This involves regular screening for MA, since urinary albumin excretion has emerged as the best maker and the most practical method for detection of early diabetic nephropathy(1).This is of clinical importance because the occurrence of persistent MA seem to predict the later development of renal failure in type 1 DM(15).

In the present work MA was detected in 36% of the patient studied which is in agreement with the previous reports(16,17,18), however, a wide variation in its prevalence (12-42%) has been reported(19,20,21).This variation may be related to the different ethnic group studied, the duration of diabetes, the degree of glycemic control and the presence of hypertension.

Although a statistical significant difference were detected in both serum urea and creatinine in patients compared to that of the control, it seems that such finding do not reflect actual deteruration in their renal functions and probably the tubulo-glomerular balance is still contact as all the diabetic children in the studied group had a mean duration of diabetes (3.2) years. The changes in glomerular functions during the course of renal disease in subjects with diabetes are difficult to evaluate because of uncertainties about the onset of diabetes and its protracted course in addition , glomerular nodular and sclerotic lesions,

become evident only in the advanced stage(22).

Concerning the glycemic control, it is obvious from table(2,3) and Figure (1) that there was a significant difference in diabetic children with and without MA as regarding the severity of DM. The association between the severity of hyperglycemia and MA was reported by certain studies(23) and the present data are in accordance with the finding of saini et al that diabetics with MA had a significant higher FPG than those without MA(24),while Nazimoon et al found a non significant difference in HbA1c. This partly be attributed to the difficulty in timing the onset of diabetes(25).

There was a significant correlation between proteinurea (as reflected by UACR) and the duration of DM ($r=0.69$, $P<0.001$, Figure2). This agrees with the finding of Patel KI and his colleagues that MA increased progressively with the duration of diabetes. It increased from 8.3% (< 5 years) to 12.6% (6-10 years) and 33.3% (<15years)(26).

In conclusion, it is obvious that the duration and severity of diabetes play an important role in decreasing the possibility of DN, regular measurement of MA (with highest priority to HbA1c as a glycemic index), MA should decline substantially which should in turn lower the number in whom over proteinuria and end-stage renal disease developed.

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Table 1 Characteristics of the subjects studied.

Clinical,anthropometric characteristic	Case (n=72)	Control (n=24)	P*-Value
	Mean ± SD (Range)	Mean ± SD (Range)	
Age (Year)	7.60 ± 2.29 (3.5 – 12.0)	7.79 ± 2.25 (4.0 – 12.0)	0.726
Fasting Plasma Glucose (mmol / L)	11.75 ± 5.39 (5.5 – 26.4)	4.08 ± 0.57 (3.3 – 5.0)	0.001
HBA1C (%)	6.99 ± 2.29 (4.0 – 12.5)	4.54 ± 0.46 (4.0 – 5.6)	0.001
Urea (mmol / L)	4.37 ± 0.97 (3.1 – 6.8)	3.66 ± 0.70 (2.6 – 5.4)	0.001
Serum Creatinine (mmol / L)	67.65 ± 20.73 (35.4 – 123.8)	43.83 ± 10.82 (30.9 – 70.7)	0.001

Urine Creatinine (mmol / L)	8.27 ± 1.27 (4.8 – 11.0)	8.08 ± 0.95 (7.0 – 10.6)	0.423
Urine Albumin (mg / L)	38.47 ± 45.87 (10.0 – 200.0)	20.58 ± 3.91 (10.0 – 28.0)	0.002
UACR (mg / mmol)	5.12 ± 7.02 (1.4 – 33.3)	2.55 ± 0.43 (1.3 – 3.5)	0.003
Duration (year)	3.22 ± 2.02 (0.5 – 9.0)	-----	
(Male / Female) Ratio	53 / 19 = 2.79	18 / 6 = 3.00	
Sex M F	53 (73.6%) 19 (26.4%)	18 (75.0%) 6 (25.0%)	0.893**

* Z-Test of two means was performed. , ** χ^2- Test was performed.

Table 2 Relationship of fasting plasma glucose with MA.

Fasting plasma glucose mmol/L	Without MA		With MA		Total No.	P-value*
	No.	Mean±SD	No.	Mean ±SD		
<7.15	6	6.55±0.25	2	6.05±0.78	8	0.531
7.15-8.25	15	7.70±0.38	2	8.11±0.19	17	0.147
> 8.25	25	11.28±2.85	22	17.29±5.7	47	0.001
Total	46	9.50±2.89	26	15.72±6.45	72	0.001

- Z-test of two means

Table 3 Relationship of glycosylated hemoglobin with MA.

HbA1C %	Without MA		With MA		Total No.	P-value*
	No.	Mean±SD	No.	Mean ±SD		
< 6.8	40	5.53±0.72	5	5.63±0.79	45	0.001
6.8-7.6	2	7.25±0.29	5	7.38±0.39	7	0.001
< 7.6	4	9.75±2.48	16	10.24±1.59	20	0.001
Total	46	5.86±1.23	26	9.13±2.32	72	0.001

* X^2-tes

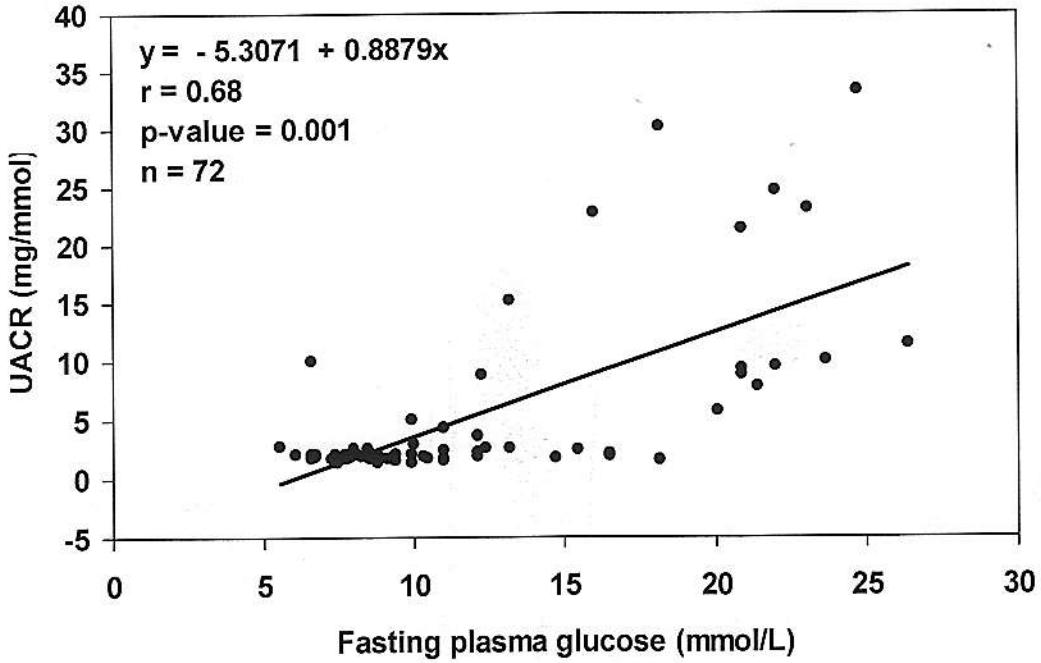

Fig. 1 Correlation between fasting plasma glucose and UACR.

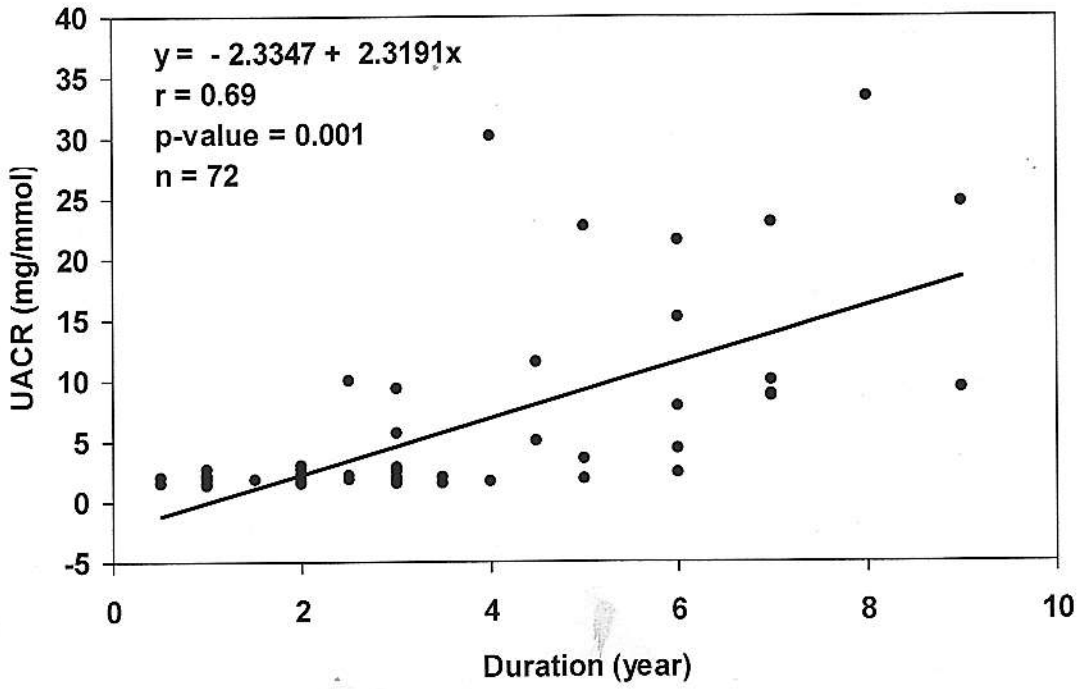

Fig. 2 Correlation between the duration of DM and UACR.