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Estimated Urinary Albumin Index: A Predictor of Microalbuminuria in Type 2 Diabetes

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This study examined factors contributing to the development of microalbuminuria in diabetic patients. A total of 236 patients with Type 2 diabetes were studied: 143 were normoalbuminuric and 86 were also normotensive. Multiple regression analysis was used to identify factors influencing the urinary albumin index (UAI), an index of proteinuria based on urinary albumin adjusted for urinary creatinine. Significant factors (retinopathy, systolic blood pressure, and glycosylated haemoglobin) were used to generate a formula for estimating the $\log_e$ UAI. Target values for systolic blood pressure and glycosylated haemoglobin to maintain the urinary albumin index at or below 22 were determined for different degrees of retinopathy. Normoalbuminuric patients were followed for 3 years to evaluate their progression to microalbuminuria. Each month, blood pressure, urinary albumin and creatinine, and glycosylated haemoglobin were measured. In normotensive, normoalbuminuric patients, initial urinary albumin index and $\log_e$ UAI were significantly higher in patients who subsequently developed microalbuminuria. Patients with initial $\log_e$ UAI > 3.09 or initial glycosylated haemoglobin > 6.0% also showed greater progression to microalbuminuria. Hyperglycaemia was an independent factor for the development of

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microalbuminuria in Type 2 diabetes. The urinary albumin index was most significantly affected by retinopathy, systolic blood pressure, and glycosylated haemoglobin. The estimated $\log_e$ UAI calculated from these factors is a useful predictor of progression to microalbuminuria.

KEY WORDS: ESTIMATED URINARY ALBUMIN INDEX; RETINOPATHY; SYSTOLIC BLOOD PRESSURE; GLYCOSYLATED HAEMOGLOBIN; MICROALBUMINURIA; TYPE 2 DIABETES

INTRODUCTION

Clinical diabetic nephropathy is defined as the development of persistent proteinuria and hypertension.[1,2] Life expectancy is shortened due to a high risk of renal failure, cardiovascular disease, or both.[1,3] Clinical diabetic nephropathy is preceded by incipient diabetic nephropathy,[4 – 8] characterized by persistent microalbuminuria. Once clinical diabetic nephropathy has developed, progression is difficult to prevent by improved metabolic control[9,10] or antihypertensive therapy.[11,12] Indeed, it has been demonstrated that strict metabolic control over 12 months does not reverse diabetic microalbuminuria.[13] The factors involved in progression from normoalbuminuria to microalbuminuria remain unclear.[5,6]

In the present study, factors contributing to the development of microalbuminuria were examined to identify means of maintaining normoalbuminuria and to clarify useful predictors of progression from normoalbuminuria to microalbuminuria.

PATIENTS AND METHODS

PATIENTS

The group initially screened for inclusion in this study were 236 patients with non-insulin-dependent diabetes mellitus (Type 2 diabetes) followed in the diabetes out-patient clinic of our hospital for a period of at least 3 months between 10 January and 30 June 1987. The diagnosis of Type 2 diabetes was based on WHO criteria. All patients were stable with regard to metabolic control, blood pressure, and other relevant parameters and had no history of cardiovascular, renal, or urinary tract disease (Table 1). In Table 1, the age given is when the patient was registered for the study, and disease duration is the period from the initial diagnosis of Type 2 diabetes until the time the patient was enrolled in the study.

PROCEDURE

Fasting morning urine samples were obtained from each patient, and albumin and creatinine concentrations were measured by immunonephelometry[14] and enzymatic analysis,[15] respectively. The urinary albumin index (UAI) was calculated as the ratio of albumin to creatinine (mg/g of creatinine) to adjust for fluctuations in urinary albumin excretion. The urinary albumin excretion rate (AER) can be calculated from the UAI using the formula $\log_e \text{AER} = 0.86 \times \log_e \text{UAI}$.[16] Patients were classified according to the definition of albuminuria adopted by our

TABLE 1

Clinical and demographic details of the study population (n = 236)

Variable	Mean ± SD	Range
Age (years)	57.0 ± 13.75	15 – 87
Height (cm)	158.5 ± 9.08	136 – 184
Weight (kg)	56.8 ± 10.07	37.8 – 100.0
Body mass index (kg/m^2)	22.5 ± 3.26	16.3 – 41.6
Disease duration (years)	7.02 ± 7.09	0 – 33
Urinary protein (g/day)	0.45 ± 0.68	0 – 2
Urinary albumin index (mg/g creatinine)	170 ± 825	0.7 – 11036
Log$_e$ urinary albumin index	3.13 ± 1.61	−0.35 – 9.3
Glycosylated haemoglobin (%)	7.47 ± 1.99	4.1 – 13.9
Blood urea nitrogen (mg/dl)	17.37 ± 5.73	7.1 – 50.6
Serum creatinine (mg/dl)	0.98 ± 1.30	0.34 – 3.0
Systolic blood pressure (mmHg)	133.8 ± 23.2	99 – 204
Diastolic blood pressure (mmHg)	75.7 ± 12.2	40 – 114

laboratory:[17,18] 143 patients showed normoalbuminuria (UAI ≤ 22 mg/g creatinine), 33 patients showed microalbuminuria (22 < UAI ≤ 50.5 mg/g creatinine) and 60 patients showed macroalbuminuria (UAI > 50.5 mg/g creatinine).

Multiple regression analysis was performed to identify the factors most closely correlated with maintenance of normoalbuminuria. Log$_e$ UAI was used as the criterion variable and 11 factors, as explanatory variables, giving a total of 12 factors in multiple regression analysis. Absolute values were used for the following explanatory variables: age (years), body mass index [kg/m^2], duration of diabetes (years), glycosylated haemoglobin (%), blood urea nitrogen (mg/dl), serum creatinine (mg/dl), and systolic blood pressure (mmHg). Qualitative explanatory variables were assigned numerical values as follows: sex, male = 0, female = 1; diabetic treatment, diet = 0, sulphonylureas = 1, insulin = 2; antihypertensive therapy, no = 0, yes = 1; and retinopathy, retinopathy-free = 0, non-proliferative retinopathy = 1, proliferative retinopathy = 2. Classification of retinopathy was based on examination at 6-month intervals by specialist diabetic ophthalmologists at our hospital. Proteinuria and diastolic blood pressure were excluded as explanatory variables because of their close correlations with UAI (r = 0.65) and systolic blood pressure (r = 0.63, Spearman's correlation factor), respectively.

PROGRESSION STUDY

To study the progression from normoalbuminuria to microalbuminuria, the 143 normoalbuminuric Type 2 diabetes patients were followed for 3 years. At baseline, these patients were classified according to WHO criteria[19] into six groups based on blood pressure and glycosylated haemoglobin (HbA_{1c}) levels:

group A_1 (n = 20)

HbA_{1c} ≤ 6.0% +hypertensive

group A_2 ($n = 9$)
$HbA_{1c} > 6.0\%$ +hypertensive

group B_1 ($n = 6$)
$HbA_{1c} \leq 6.0\%$ +borderline hypertensive

group B_2 ($n = 22$)
$HbA_{1c} > 6.0\%$ +borderline hypertensive

group C_1 ($n = 23$)
$HbA_{1c} \leq 6.0\%$ +normotensive

group C_2 ($n = 63$)
$HbA_{1c} > 6.0\%$ +normotensive.

Glycosylated haemoglobin values were determined by high-performance liquid chromatography and an automated analyser (Kyoto Daiichi Kagaku, Kyoto, Japan). Systolic and diastolic blood pressures were measured over the brachial artery with a standard mercury sphygmomanometer (cuff size: 25 cm × 12 cm) after approximately 90 min supine rest.

These patients were then monitored at monthly visits, where blood pressure was measured and fasting blood and urine samples were collected. Urinary albumin and creatinine, and glycosylated haemoglobin were measured as described above. UAI and urinary albumin excretion rate were calculated and used to classify each patient as normo-, micro-, or macroalbuminuric, as described above, after ruling out urinary tract infection and other disorders known to increase urinary protein excretion. If microalbuminuria was consistently recorded at each visit after the initial diagnosis, persistent microalbuminuria was diagnosed. Clinical diabetic nephropathy was defined as Albustix®-positive (Bayer-Sankyo Co Ltd, Tokyo, Japan).

STATISTICAL ANALYSIS

A P value of less than 0.05 was considered statistically significant. The χ^2 test was applied when appropriate.

RESULTS

Multiple regression analysis with $\log_e$ UAI as the criterion variable and other factors as explanatory variables showed that the explanatory variables with the greatest weights were diabetic retinopathy, systolic blood pressure (SBP) and glycosylated haemoglobin (HbA_{1c}) in that order ($n = 235$, $R^2 = 0.4079$, $P = 0.0001$; Table 2). The other explanatory variables were not statistically significant. Using these three significant variables, multiple regression analysis was repeated and the following formula was obtained:

$$\text{estimated } \log_e \text{UAI} = (0.88439 \times \text{retinopathy}) + (0.02328 \times \text{SBP}) + (0.17935 \times \text{HbA}_{1c}) - 1.61848 \quad (1)$$

The relationship between systolic blood pressure and the glycosylated haemoglobin level was examined using formula (1) to clarify how these factors might relate to maintaining a normoalbuminuric UAI value (Fig. 1).

Seven (4.9%) of the 143 normoalbuminuric patients dropped out of the study for reasons such as change of residence or employment. During the 3-year follow-up period, retinopathy developed in none of our patients, and persistent microalbuminuria developed in 36 (26.5%) of the remaining 136 patients (3 of 19 in group A_1, 3 of 8 in group A_2, 0 of 5 in group B_1, 9 of 22 in group B_2, 1 of 21 in group C_1, and 20 of 61 in group C_2), but not in the other 100 (73.5%). There were no patients in whom the development of proteinuria was questionable, and none developed fatal uraemia. The identification of microalbuminuria was not difficult because only normoalbuminuric patients were selected initially and urinalysis was repeated at short (1-month) intervals, permitting accurate timing of the onset of persistent microalbuminuria. The mean interval

TABLE 2

Multiple regression analysis with log$_e$ urinary albumin index (UAI) as the criterion variable and the other 11 factors as explanatory variables

Parameters	Coefficient	Standard error	T value	*P* value
Log$_e$ UAI (intercept)	−2.1108	0.8863	−2.382	0.0181
Sex	−0.0829	0.1847	−0.449	0.6540
Age	0.0056	0.0078	0.716	0.4747
Body mass index	0.0006	0.0285	0.020	0.9841
Disease duration	0.0039	0.0158	0.247	0.8048
Glycosylated haemoglobin	0.1589	0.0457	3.474	0.0006
Diabetes drug use	0.1356	0.1283	1.056	0.2920
Antihypertensive drug use	0.3952	0.2514	1.572	0.1174
Blood urea nitrogen	0.0248	0.0195	1.275	0.2038
Serum creatinine	0.5074	0.3656	1.388	0.1666
Retinopathy	0.6734	0.1569	4.292	0.0001
Systolic blood pressure	0.0179	0.0048	3.728	0.0002

$n = 235$ (one patient excluded due to insufficient data); $r^2 = 0.4079$; $P = 0.0001$.

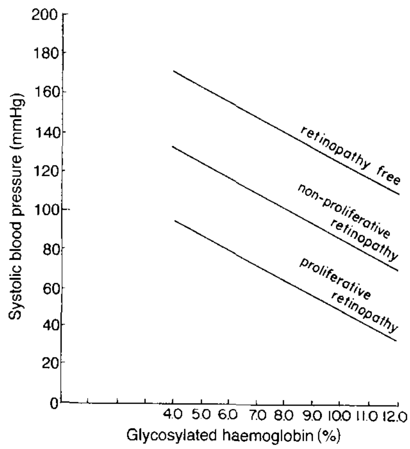
between the start of the study and the appearance of persistent microalbuminuria was 0.96 ± 0.81 years.

Groups A and B were too small, so statistical analysis was applied only to patients in group C. In the 82 normoalbuminuric, normotensive patients, the prognostic value of the initial glycosylated haemoglobin level was evaluated by examining the time-course of the glycosylated haemoglobin level compared with the initial glycosylated haemoglobin level. Glycosylated haemoglobin values were higher in the group with high initial glycosylated haemoglobin levels (group C_2, $n = 61$) than in the group with normal initial glycosylated haemoglobin levels (group C_1, $n = 21$) at all examination times (Fig. 2). The prognostic value of the initial log$_e$ UAI or estimated log$_e$ UAI was examined in a similar way. Log$_e$ UAI or estimated log$_e$ UAI was higher in the group with high initial glycosylated haemoglobin levels than in those with normal initial glycosylated haemoglobin levels at all examination times (Fig. 3). These results suggest that a high initial glycosylated haemoglobin level may indicate subsequent persistently higher glycosylated haemoglobin levels and log$_e$ UAI. Systolic blood pressure did not differ significantly between the groups with high and normal initial glycosylated haemoglobin levels (Fig. 4).

In normotensive, normoalbuminuric patients, both the initial UAI and the calculated UAI were significantly higher in the 21 patients who later developed persistent microalbuminuria (UAI 10.65 ± 1.57; estimated UAI 19.09 ± 2.25) than in the 61 patients who did not (UAI 5.64 ± 3.13; estimated UAI 13.29 ± 1.73; $P < 0.02$ and $P < 0.05$, respectively).

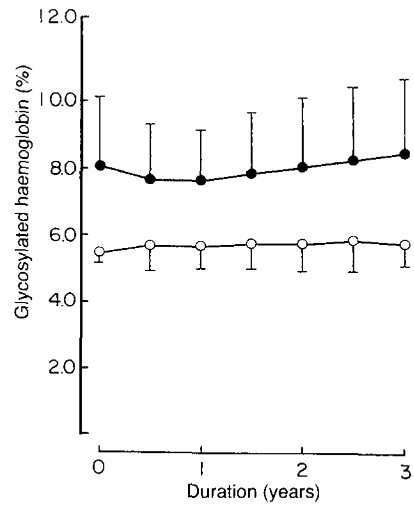
For the 82 normoalbuminuric, normotensive patients at the start of the study, initial estimated log$_e$ UAI was calculated from the

FIGURE 1



The relationships between systolic blood pressure and glycosylated haemoglobin levels based on formula (1), needed to maintain the urinary albumin index at 22 or less, in patients with proliferative retinopathy, non-proliferative retinopathy and no retinopathy.

FIGURE 2

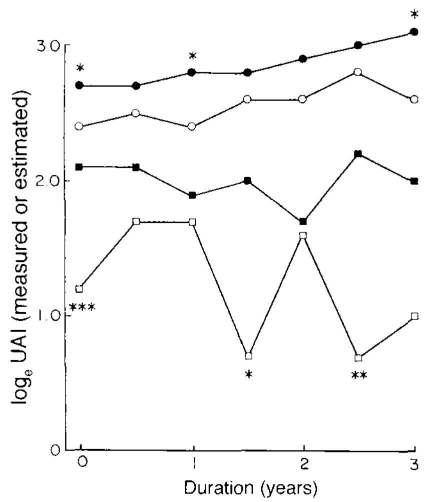


Time-course of changes in glycosylated haemoglobin levels, for normotensive, normoalbuminuric patients with normal initial glycosylated haemoglobin levels (○: group C_1; n = 21) or with high initial glycosylated haemoglobin levels (●: group C_2; n = 61).

retinopathy score, systolic blood pressure, and glycosylated haemoglobin level using formula (1). The patients were then divided into two groups: an estimated microalbuminuria group in which the initial estimated $\log_e$ UAI was > 3.092 and an estimated normoalbuminuria group in which the initial estimated $\log_e$ UAI was ≤ 3.092. The incidence of persistent microalbuminuria at later times was then examined. According to formula (1), the glycosylated haemoglobin level should be higher in patients with initial estimated microalbuminuria, suggesting that these patients are likely to progress to microalbuminuria. The results showed that the incidence of persistent microalbuminuria was higher in patients with initial estimated microalbuminuria than in those with initial estimated normoalbuminuria (Fig. 5), supporting the hypothesis that in normoalbuminuria, hyperglycaemia may be an independent factor for the development of microalbuminuria in normotensive patients.

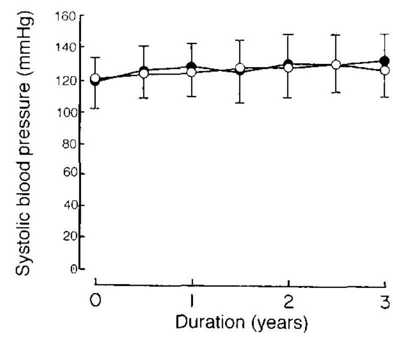
To further clarify the role of the glycosylated haemoglobin level as a contributory factor in progression to microalbuminuria, the cumulative incidence of persistent microalbuminuria at the end of the study was compared with the HbA_{1c} level in the normotensive state. The incidence of persistent microalbuminuria was significantly higher in the group with high initial glycosylated haemoglobin levels (32.8%) than in the group with normal initial glycosylated hae-

FIGURE 3



*Time-course of changes in estimated $\log_e$ urinary albumin index (UAI) and $\log_e$ UAI, for different initial glycosylated haemoglobin (HbA_{1c}) levels in 82 normotensive normoalbuminuric patients. ○: estimated $\log_e$ UAI in normal initial HbA_{1c} group (group C_1, n = 21); ●: estimated $\log_e$ UAI in high initial HbA_{1c} group (group C_2, n = 61); □: $\log_e$ UAI in normal initial HbA_{1c} group, ■: $\log_e$ UAI in high initial HbA_{1c} group. *$P < 0.05$, **$P < 0.02$, ***$P < 0.01$.*

FIGURE 4



Time-course of changes in systolic blood pressure for different initial glycosylated haemoglobin (HbA_{1c}) levels in 82 normotensive, normoalbuminuric with normal initial glycosylated haemoglobin levels (○: group C_1; n = 21), or with high initial glycosylated haemoglobin levels (●: group C_2, n = 61).

moglobin levels (4.8%) ($P < 0.05$, χ^2 test; Fig. 6).

DISCUSSION

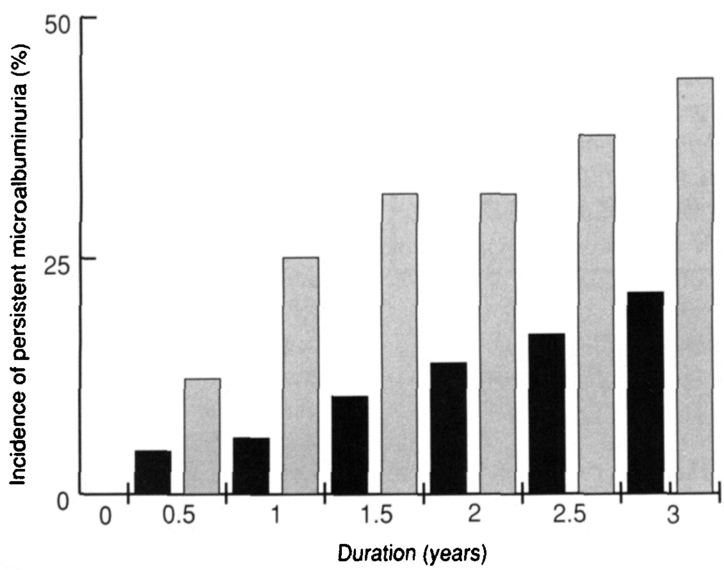
The parameters evaluated in the present study are reviewed first. The development of microalbuminuria[14] is a reliable marker for the early detection of diabetic nephropathy, even when Albustix® tests remain negative.[3] The urinary albumin excretion rate (AER) is calculated from the measured urinary albumin level, with the normal range defined as ≤ 15 μg/min for insulin-dependent diabetes mellitus (Type 1 diabetes). In previous studies, we generated the formula $\log_e$ AER = 0.86 × $\log_e$ UAI based on morning random urine samples ($P < 0.0001$).[16] Since the normal range for UAI in adults is known to be ≤ 22,[17] the normal range for AER can be calculated to be ≤ 14.2 μg/min. The cut-off point between microalbuminuria and macroalbuminuria was found to be UAI=50.5.[18] Thus, UAI and AER ranges corresponding to the microalbuminuric state were 22 < UAI ≤ 50.5 mg/g creatinine and 14.2 < AER ≤ 29.2 μg/min.

To prevent diabetic nephropathy, the levels of relevant parameters of diabetes should be controlled to maintain UAI ≤ 22. In the present study, the most significant explanatory variables for $\log_e$ UAI were retinopathy, systolic blood pressure, and glycosylated haemoglobin level, in that order. This suggests that it is particularly important to monitor the systolic blood pressure and glycosylated haemoglobin level to prevent diabetic nephropathy, and that the goal of controlling diabetes mellitus should be to maintain these factors at levels that maintain a UAI ≤ 22.

Repeated multiple regression analysis using the above three significant explanatory variables resulted in formula (1). Using this formula, the target level of systolic blood pressure needed to maintain UAI ≤ 22 can be determined. For example, in a patient with a glycosylated haemoglobin level of 7% and no retinopathy, the target systolic blood pressure is ≤ 148 mmHg. Figure 1 shows, on the basis of formula (1), the relationships between glycosylated haemoglobin level and systolic blood pressure to meet the conditions for UAI ≤ 22 in patients with proliferative retinopathy, nonproliferative retinopathy, and no retinopathy. The values of glycosylated haemoglobin and systolic blood pressure required to satisfy UAI ≤ 22 can only be achieved in retinopathy-free patients in clinical practice.

Even in normotensive, normoalbuminuric patients, a higher initial estimated $\log_e$ UAI (> 3.092, *initial estimated microalbuminuria*) indicates a higher risk of progression to microalbuminuria, since higher glycosylated haemoglobin values are expected in patients with higher initial estimated microalbuminuria compared with those with lower initial estimated $\log_e$ UAI (≤ 3.092, initial estimated normoalbuminuria). The results of the

FIGURE 5



Time-course of the incidence of persistent microalbuminuria in groups in which the initial estimated $\log_e$ urinary albumin index was ≤ 3.092 (■; n = 66) or > 3.092 (▧; n = 16) in 82 normotensive, normoalbuminuric patients.

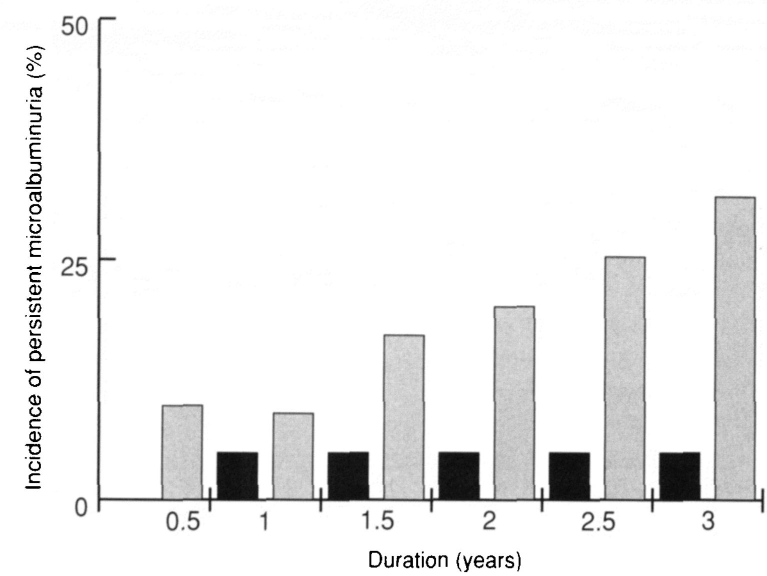
present study are consistent with this expectation (Fig. 5), and help to verify the legitimacy of formula (1) for estimating UAI.

The cumulative incidence of persistent microalbuminuria in normotensive, normoalbuminuric patients was significantly higher in patients with higher initial glycosylated haemoglobin values, suggesting that the hyperglycaemic state is an independent contributor to progression to persistent microalbuminuria. Thus, strict metabolic management must be initiated as early as possible to prevent the development of diabetic nephropathy in patients with Type 2 diabetes.

A similar tendency with respect to glycosylated haemoglobin was observed in normoalbuminuric patients with hypertension and with borderline hypertension. Because the number of subjects was small in the present study, statistical analysis could not be applied with respect to the weight of hypertension as a contributor to the development of microalbuminuria. This point needs to be studied in more detail. However, the present study demonstrates that hypertension is not an essential factor in the progression from normoalbuminuria to persistent microalbuminuria, but that hyperglycaemia is a contributory factor in normotensive patients.

A 5-year prospective study in 205 normotensive normoalbuminuric patients with Type 1 diabetes showed that initial urinary albumin excretion and glycosylated haemoglobin levels were significantly higher in 15 patients who later developed microalbumin-

FIGURE 6



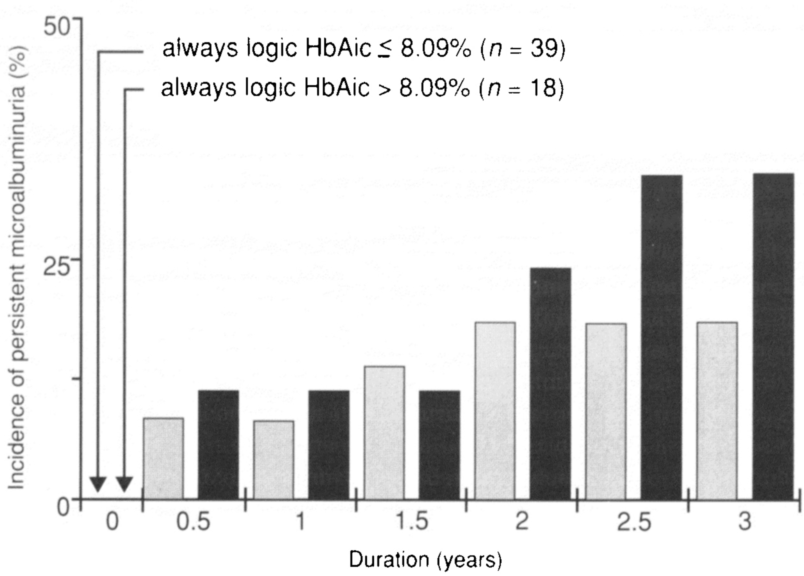
Time-course of the incidence of persistent microalbuminuria in groups in which the initial glycosylated haemoglobin level was ≤ 6.0% (■; n = 21) and > 6.0% (▒; n = 61) in 82 normotensive, normoalbuminuric patients.

uria than in 190 who remained normoalbuminuric, but the initial blood pressure did not differ significantly between the two groups.[20] Our 3-year prospective pilot study involving 82 normotensive, normoalbuminuric patients with Type 2 diabetes showed similar results: initial glycosylated haemoglobin levels UAI, and estimated UAI values were significantly higher in the 21 patients who developed microalbuminuria than in the 61 who remained normoalbuminuric. There was no significant difference in initial systolic blood pressure between the two groups. These results justify the use of formula (1).

Is it possible to prevent diabetic nephropathy with strict metabolic control? The incidence of persistent microalbuminuria in patients maintaining glycosylated haemoglobin levels ≤ 8.09% (calculated from formula (1) for a systolic blood pressure of 140 mmHg) or estimated $\log_e$ UAI ≤ 3.092 over the entire period of our study was lower than that in those with glycosylated haemoglobin levels > 8.09% or estimated $\log_e$ UAI > 3.092 (Fig. 7). Progression to persistent microalbuminuria was less frequent for estimated UAI ≤ 22, than for estimated UAI > 2, indicating that nephropathy may be prevented by maintaining the glycosylated haemoglobin level, estimated from formula (1), within an acceptable range.

This study has clarified the target levels for various parameters of diabetic control to prevent diabetic nephropathy and has also demonstrated that hyperglycaemia is an independent factor responsible for the devel-

FIGURE 7



Time-course of the incidence of persistent microalbuminuria in groups in which the glycosylated haemoglobin (HbA_{1c}) level remained ≤ 8.09% (■; estimated range for $\log_e$ UAI ≤ 3.092; n ***= 39) and in which the HbA_{1c} remained > 8.09% (░; estimated range for $\log_e$ UAI ≤ 3.092;*** n ***= 18) in 82 normotensive, normoalbuminuric patients.***

opment of microalbuminuria in Type 2 diabetes. The results of this study provide not only a useful predictor of progression to microalbuminuria, but also useful guidelines for the day-to-day management of patients with Type 2 diabetes, with the ultimate goal of preventing the development of diabetic nephropathy.

REFERENCES

1 Deckert T, Poulsen JE, Larsen M: Prognosis of diabetics with diabetes onset before the age of thirty-one. 1. Survival, causes of death and complications. *Diabetologia* 1978; **28:** 590 – 596.

2 Andersen AR, Christiansen JS, Andersen JK, *et al*: Diabetic nephropathy in type 1 (insulin-dependent) diabetes: an epidemiological study. *Diabetologia* 1983; **25:** 496 – 501.

3 Mogensen CE: Microalbuminuria predicts clinical proteinuria and early mortality in maturity onset diabetes. *N Engl J Med* 1984; **310:** 356 – 360.

4 Mogensen CE, Christensen CK, Vittinghus E: The stages in diabetic renal disease. With emphasis on the stage of incipient nephropathy. *Diabetes* 1983; **32** (Suppl 2): 64 – 78.

5 Viberti CG, Hill RD, Jarrett RJ, *et al*: Microalbuminuria as a predictor of clinical nephropathy in insulin-dependent diabetes mellitus. *Lancet* 1982; **i:** 1430 – 1432.

6 Parving H-H, Oxenboll B, Svendsen PA, *et al*: Early detection of patients at risk of developing diabetic nephropathy: a longitudinal study of urinary albumin excretion. *Acta Endocrinol (Copenh)* 1982; **100:** 550 – 555.

7 Mathiesen ER, Oxenboll B, Johansen K, *et al*: Incipient nephropathy in type 1 (insulin-dependent) diabetes. *Diabetologia* 1984; **26:** 406 – 410.

8 Mogensen CE, Christiansen CK: Predicting diabetic nephropathy in insulin-dependent patients. *N Engl J Med* 1984; **311:** 89 – 93.

9 Krolewski AS, Canessa M, Rand LI: Genetic predisposition to hypertension as a major determinant of development of diabetic nephropathy. *Kidney Int* 1987; **31:** 388.

10 Hilton PJ: Cellular sodium transport in essential hypertension. *N Engl J Med* 1986; **314:** 222 – 229.

11 Viberti GC, Mackintosh D, Bilous RW, *et al*: Proteinuria in diabetes mellitus: role of spontaneous and experimental variation of glycemia. *Kidney Int* 1982; **21:** 714 – 720.

12 Viberti GC, Mackintosh D, Keen H: Determinants of the penetration of proteins through the glomerular barrier in insulin-dependent diabetes mellitus. *Diabetes* 1983; **32** (Suppl 2): 92 – 95.

13 Feldt-Rasmussen B, Mathiesen ER, Hegedus L, *et al*: Kidney function during 12 months of strict metabolic control in insulin-dependent diabetic patients with incipient nephropathy. *N Engl J Med* 1986; **314:** 665 – 670.

14 Harmoinen A, Vuorinen P, Jokela H: Turbidimetric measurement of microal-

buminuria. *Clin Chim Acta* 1987; **166:** 85 – 89.

15 Miller BF, Dubos R: Determination by a specific, enzymatic method of the creatinine content of blood and urine from normal and nephritic individuals. *J Biol Chem* 1937; **121:** 457 – 464.

16 Okada S, Ichiki K, Tanokuchi S, *et al*: To what extent does urinary albumin index contribute to estimation of albumin excretion rate in patients with non-insulin-dependent diabetes mellitus? In: *Prevention and Treatment of NIDDM* (Goto Y, Lee TH, Kaneko T, *et al*, eds). London: Smith-Gordon Publisher, 1992; pp 311 – 312.

17 Okada S, Ichiki K, Tanokuchi S, *et al*: The range of urinary albumin index in normoalbuminuria. *J Diabetic Complications* 1991; **5:** 153 – 154.

18 Okada S, Ichiki K, Tanokuchi S, *et al*: Determination of a cut-off point between treatable and untreatable ranges of nephropathy estimated from the urinary albumin index (UAI) in non-insulin-dependent diabetes mellitus (NIDDM). In: *Recent Trends of Diabetes Mellitus in East Asia* (Mimura G, Zhisheng C, eds). Amsterdam: Elsevier Science Publishers, 1990; pp 239 – 342.

19 Report of a WHO Expert Committee: Arterial hypertension. World Health Organ Tech Rep Ser, Geneva: WHO, 1978; p 628.

20 Mathiesen ER, Ronn B, Jensen T, *et al*: Relationship between blood pressure and urinary albumin excretion in development of microalbuminuria. *Diabetes* 1990; **39:** 245 – 249.

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