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Assessment of microalbuminuria and glycated hemoglobin in type 2 diabetes mellitus complications

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ABSTRACT

Objective: To relate microalbuminuria with the degree of glycaemic control in type 2 diabetic patients and determine the prevalence of poor glycaemic control amongst the normotensive diabetes mellitus (NDM) and hypertensive diabetes mellitus (HDM) with or without microalbuminuria. **Methods:** A total of 95 type 2 diabetes mellitus patients and 30 healthy controls were randomly selected and studied. 17 of the 95 patients were normotensive diabetic with microalbuminuria, 40 of them were HDM presenting with microalbuminuria and 38 were NDM without microalbuminuria. Their blood was obtained for fasting plasma glucose and glycated haemoglobin while their urine was obtained for albumin and creatinine estimation and the ratio was calculated. **Results:** Out of the 95 diabetic patients studied, 57 (60%) of them had microalbuminuria while 38 (40%) had normoalbuminuria. The mean ages in the diabetics with microalbuminuria were higher than those without microalbuminuria ($P=0.0546$). The mean glycated haemoglobin was the highest ($5.95\pm 2.06\%$) in NDM with microalbuminuria when compared with HDM with microalbuminuria ($5.83\pm 1.62\%$) and that in ($5.66\pm 2.49\%$) in NDM without microalbuminuria ($P=0.0009$). Similarly, fasting plasma glucose was the highest (9.09 ± 4.31) mmol/L in NDM with microalbuminuria than those without microalbuminuria (7.70 ± 3.33) mmol/L ($P=0.0001$). The prevalence of poor glycaemic control was the highest (29%) in NDM with microalbuminuria while the least (21%) in NDM without microalbuminuria. **Conclusions:** The risk of microalbuminuria increases with poor glycaemic control. Persistent increase in glycated haemoglobin may be an indicator of worsening albumin creatinine ratio and diabetic nephropathy. Therefore, regular screening for microalbuminuria in addition to continuous (3-monthly) glycated HbA1c estimation is advised.

1. Introduction

The major clinical objective in the management of diabetes mellitus (DM) is to control hyperglycemia and the specific long term objectives are to prevent microvascular and macrovascular complications[1]. The control of blood glucose levels in patients with DM is important in preventing long term complications. Poor glycaemic control has been identified as one of the risk factors of microalbuminuria (incipient nephropathy) which hastens the progress of renal disease[2]. The pathophysiologic basis for elevated urinary albumin excretion entails the binding of glucose to proteins resulting in excessive protein glycosylation with the build-up of advanced glycosylated end products. This is encoded by the transcription of the gene for transforming growth factor- β (TGF- β), which is stimulated by hyperglycemia,

resulting in the upregulation of glucose transport 1 (GLUT-1) in the mesangial cells[3]. This leads to deposition of advanced glycosylated end products on the glomerulus which are recognised by receptors for the advanced glycosylated end products (RAGE), selectively expressed on the glomerular epithelial cells (podocytes)[3,4]. The resultant effect is the thickening of the glomerular capillaries, accumulation of mesangial basement membrane (excess extracellular matrix proteins), deposition of fibrin and increased vascular permeability. This abnormality permits the leakage of low molecular weight proteins (albumin)[4]. This is the stage of microalbuminuria (incipient nephropathy) which could be reversible with good glycaemic control. However, with persistent microalbuminuria, further leakage of protein in the urine will result in overt diabetic nephropathy. Over the years, glycaemic control has been measured through testing for glycated haemoglobin, specifically HbA1c. This is the preferred standard tool for assessing glycaemic control over previous 2–3 months. The target for glycaemic control of HbA1c value $<7\%$ was based on findings from several clinical trials[5]. According to previous studies[5,6]

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measuring glycated haemoglobin may be useful in determining the severity of diabetes. The basis of its use in diagnostic measurement is as follows. Hemoglobin is a protein molecule found in red blood cells, when glucose binds to it, glycation occurs. This affects the number of patients and an elevated level of glycated haemoglobin is strongly associated with poor glycaemic control. Glycated haemoglobin of 1% above normal range identifies diabetes in 98% of patients. However, normal HbA1c levels do not rule out diabetes, but in diabetes with normal values, the risk of complication is low. Values >7% indicate poor control of glucose and are a marker of renal disease[7]. These groups of patients were found to have an unadjusted increased risk of microalbuminuria up to 3–9 times in type 1 and 1.4–8 times in type 2 DM[7]. It was then concluded that the risk of microalbuminuria increases abruptly when HbA1c rises above 8.1% suggesting that efforts to reduce frequency of diabetic nephropathy should also be focussed on reducing HbA1c.

2. Materials and methods

A total of 95 type 2 DM patients aged between 25–70 years were randomly selected from the registered diabetic patients attending the Medical Outpatient Department of the University of Benin Teaching Hospital, Benin City. The patients were classified into four groups using the urine albumin: creatinine ratio (ACR) levels and blood pressure. Subjects with urine ACR>30 mg/g and ACR<30 mg/g were assumed to have microalbuminuria and normoalbuminuria, respectively. Groups A: Normotensive diabetes presenting with microalbuminuria (NDM) ($n=17$). Group B: Hypertensive diabetics with microalbuminuria (HDM) ($n=40$). Group C: Normotensive diabetics without microalbuminuria (ND) ($n=38$). Group D: Non-diabetics normotensive (controls) without microalbuminuria ($n=30$). The controls were of the same age range as the patients and were drawn from the hospital staff. All participants gave informed written consent after due explanation by the researchers. Ethical clearance was sought and obtained from the Hospital Research and Ethics Committee. Their biodata, body weight (kg), height (m) and blood pressure (mmHg) were obtained. Heights were measured to 0.1 cm free standing against a marked wooden ruler in (cm). Weights were measured to 0.1 kg without shoes and minimal clothing using a flat weighing scale (Hop-on-Hanson model). Blood pressure was measured using a mercury sphygmomanometer and hypertension was defined as BP>140/90 mmHg. Body mass index (BMI) was calculated using the formula: weight (kg) / height (m)². BMI <19 = Underweight, 19–25 =normal weight, 25–30 = overweight, >30=obesity[8]. Fasting plasma samples were obtained for blood glucose and glycated haemoglobin. Blood glucose was determined by glucose oxidase method[9], glycated haemoglobin by fast ion exchange resin separation

method[10] and urine albumin by Folin–Lowry method[11] and creatinine by modified Jaffe method[12].

Data obtained from this study were grouped and analysed by tables using SPSS version 13.0.0. Means and standard deviations were determined for quantitative data and frequency determined for categorical variables. Student's *t*-test was used to test for significant association between two means, ANOVA was used to compare multiple means, while *Chi*-squared test was used to analyse group differences for categorical variables. Bar chart was used to express frequency distribution. All tests were carried out at 5% frequency distribution.

3. Results

Amongst the 95 diabetics studied, 57 (60%) of them had microalbuminuria while 38 (40%) of them were without microalbuminuria. The baseline characteristics of the studied groups according to degree of albuminuria were summarized in Table 1. The mean glycated Hb was the highest (5.95 ± 2.06)% in normotensive diabetics with microalbuminuria compared with (5.83 ± 1.62)% in hypertensive diabetics with microalbuminuria, (5.66 ± 2.49)% in ND and it was the least (4.16 ± 0.83)% in the control ($P=0.0009$). In a similar fashion, fasting plasma glucose is highest in NDM with microalbuminuria and lowest in those without microalbuminuria ($P=0.0001$).

In Table 2, the two extremes of glycemic controls were described for all diabetic patients studied. In all, the diabetics with microalbuminuria had higher mean values in both the good glycemic category (HbA1c <7%) and the poor glycemic category (HbA1c >7%) when compared with the diabetics without microalbuminuria ($P>0.05$).

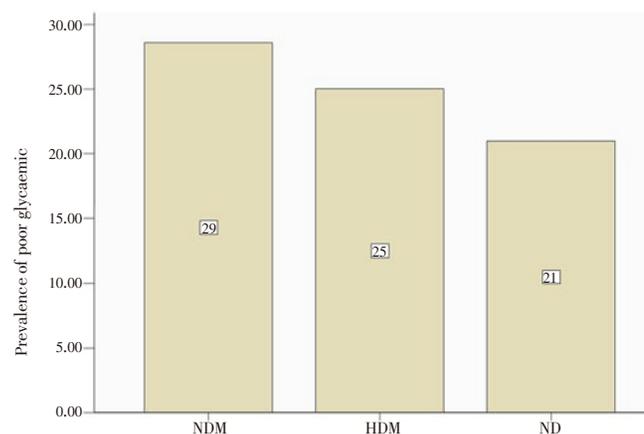


Figure 1. Frequency of poor glycaemic control in the studied groups.

The prevalence of poor glycaemic control was found to be the highest (29%) in the NDM with microalbuminuria compared with the HDM with microalbuminuria (25%) and

Table 1

Baseline characteristics of type 2 DM with complications (Mean±SD).

Parameters	NDM	HDM	ND	Control	<i>P</i> -value
Age (years)	57.40±10.05	56.80±9.24	53.80±9.80	50.20±10.20	0.0546
BMI (kg/m ²)	25.00±4.27	26.90±5.65	25.30±4.22	25.40±4.73	0.3832
SBP (mmHg)	133.50±26.40	158.40±16.70	121.20±11.60	118.00±8.33	0.0001
DBP (mmHg)	81.20±12.70	92.00±8.30	78.70±9.05	75.00±6.88	0.0001
FPG (mmol/L)	9.09±4.31	7.89±3.82	7.70±3.33	4.92±0.61	0.0001
HbA1c (%)	5.95±2.06	5.83±1.62	5.66±2.49	4.16±0.83	0.0009

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HbA1c: Glycated haemoglobin.

Table 2

The mean glycosylated haemoglobin values of the diabetic patients based on the degree of glycaemic control (Mean±SD).

Degree of glycaemic control	NDM	HDM	ND	P-value
Good glycaemic control (<7%)	5.05±1.17	5.12±1.11	4.60±1.32	0.228 7
Poor glycaemic control (>7%)	8.87±1.49	7.94±0.91	8.40±0.80	0.277 0

that (21%) in the DM without microalbuminuria (Figure 1). It showed that a large proportion (49, 75.4%) of the diabetics (normotensive and hypertensive) with microalbuminuria and (24, 80%) of the DM without microalbuminuria had good glycaemic control. However, the percentage of poor glycaemic control was higher (16, 24.6%) amongst those with microalbuminuria than (6, 20%) in those without microalbuminuria ($\chi^2 = 0.7168$, DF = 1, $P = 0.1986$).

4. Discussion

The higher mean age of DM with microalbuminuria suggests that this complication occurs at later duration of the disease which is in keeping with previous report of (10.30±0.50) years of duration of disease diagnosis at the time of first visit^[13]. The higher mean value of glycosylated haemoglobin in the complicated diabetes was expected in view of the presence of microalbuminuria in majority of the DM patients studied. This is based on previous fact that HbA1c can provide an accurate and reliable method to routinely assess the relative level of diabetes control. Level of mean blood glucose, effectiveness of treatment and risk of development of possible long term chronic complications are typically associated with suboptimal or poor glycaemic control in complicated diabetics^[14]. This finding was also supported by an evidenced based study which showed a graded relationship between HbA1c and the risk of nephropathy in type 1 and type 2 DM patients^[7]. These patterns were observed for various measures of HbA1c, HbA1b and total Hb.

We also observed in this study, that the highest percentage of frequency (29%) of poor glycaemic control in diabetics presenting with microalbuminuria as against those without microalbuminuria (21%) may be supportive of the previous findings of the 2–8 times magnitude risk of microalbuminuria in type 2 DM patients due to poor glycaemic control. There is relative risk reduction, when the mean HbA1c is maintained at approximately 7% compared with randomised glycaemia control of up to 9%^[5,7]. The risk of microalbuminuria increases with poor glycaemia control. Persistent increase in glycosylated haemoglobin may be an indicator of worsening albumin creatinine ratio and diabetic nephropathy.

From the foregoing, it is obvious that good glycaemia control is the key to preventing and/or forestalling microalbuminuria and subsequently, diabetic nephropathy amongst other chronic complications of DM. Therefore, regular screenings for microalbuminuria in addition to continuous (3-monthly) glycosylated HbA1c estimation are important tools in the management of DM.

Patients and health care givers should give very high priority to improving glycaemia control sufficiently to maintain blood glucose. If this is achieved, the number of patients with microalbuminuria will decline substantially and in turn lower numbers in which overt macroalbuminuria and end stage renal disease develop.

We declare that we have no conflict of interest.

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References

- [1] American Diabetes Association. Report on the expert committee on the diagnosis and classification of DM: clinical practice recommendations. *Diabetes Care* 2000; **21**(Suppl 11): S5–S19.
- [2] Perrin NE, Torbjornsdotter T, Jaremko GA, Berg UB. Risk markers of future micro albuminuria and hypertension based on clinical and morphological parameters in young type 1 diabetic patients. *Pediatr Diabetes* 2010; **11**(5): 305–313.
- [3] Qian Y, Feldman E, Pennathur S, Kretzler M, Brosius FC. Mechanism of glomerulosclerosis in diabetic nephropathy. *Diabetes* 2008; **57**: 1439–1445.
- [4] Roestenberg P. *Diabetes nephropathy and the pathogenic role of growth factors*. [Online] Available from: www.NIER(nephrological issues in Experimental Research).org. 2006. [Accessed on 22 Jan, 2007]
- [5] Stolar M. Glycaemic control and complications in types 2 diabetes mellitus. *Am J Med* 2010; **123**(3): S3–S11.
- [6] Redon J. Measurement of micro albuminuria—what the nephrologists should know. *Nephrol Dial Transplant* 2006; **21**(3): 573–576.
- [7] Vergouwe Y, Soedamah–Muthu SS, Zgibor J, Chaturvedi N, Forsblom C, Snell–Bergeon JK, et al. Progression to microalbuminuria in type 1 diabetes: development and validation of a prediction rule. *Diabetologia* 2010; **53**: 254–262.
- [8] Ofoegbu EN, Oli JM, Igweh JC. Body composition of Nigerian diabetics using Bioimpedence analysis. *Niger J Health Biomed Sci* 2004; **3**(1): 37–39.
- [9] Braham D, Trinder P. An improved colour reagent for the determination of blood glucose by glucoseoxidasesystem. *Analyst* 1972; **97**: 142–145.
- [10] Nuttal FQ. Glycohemoglobin HbA1 assay, fast ion–exchange resin separation method. *Manual of analysis human laboratories*. Wiesbaden: 1998, p. 1475–1480.
- [11] Lowry OH, Rosebrough NJ, Randall RJ. Protein measurement with the Folin phenol reagent. *J Biol Chem* 1951; **193**: 265–275.
- [12] Gary LM, Miller WG, Josef C, James F, Neil G, Tom G, et al. Recommendation for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem* 2006; **52**: 5–18.
- [13] Amanda IA, Richard TS, Sue Em, Rudy WB, Carole AC, Rury RH. Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS64). *Kidney Int* 2003; **63**: 225–232.
- [14] Genuth S. Insight from the diabetes control and complications trial/epidemiology of diabetes interventions and complications study on the use of intensive glycaemic treatment to reduce the risk of complications of type 1 diabetes. *Endocr Pract* 2006; **12**: 34–41.

Conflict of interest statement