British Journal of Medicine & Medical Research
9(2): 1-6, 2015, Article no.BJMMR.18128
ISSN: 2231-0614

SCIENCEDOMAIN *international*
www.sciencedomain.org

Moderately Increased Albuminuria; Marker of Chronic Complications in Nigerian Diabetes Mellitus Type 2 Patients; Makurdi Perspective

B. K. Myke-Mbata[1], S. C. Meludu[2], C. E. Dioka[2], S. A. Adebisi[1], E. K. Oghagbon[1], G. I. Achinge[3], C. E. Onah[4*] and B. O. Onyemailo[4]

[1]Department of Chemical Pathology, Faculty of Basic and Allied Sciences, Benue State University, Markurdi, Benue State, Nigeria.
[2]Department of Chemical Pathology, Faculty of Medicine, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria.
[3]Department of Medicine, Faculty of Clinical Sciences, Benue State University, Markurdi, Benue State, Nigeria.
[4]Department of Chemical Pathology, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author BKMM originated the concept, wrote the protocol, the first draft and collected data. Authors SCM, CED, EKO and SAA performed critical reviews of the manuscript. Authors BKMM and EKO managed the literature searches. Authors CED, GIA and BOO performed the data analysis. All authors approved of the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2015/18128
Editor(s):
(1) Kate S. Collison, Department of Cell Biology, King Faisal Specialist Hospital and Research Centre, Saudi Arabia.
Reviewers:
(1) Shannon Doherty Lyons, Department of Environmental Medicine, New York University School of Medicine, USA.
(2) Saadia Shahzad Alam, Department of Pharmacology and Therapeutics, Shaikh Zayed Medical Complex, Pakistan.
(3) Anonymous, Madurai Kamaraj University, India.
(4) Giancarlo Tonolo, Hospital San Giovanni di Dio, Olbia, Italy.
(5) Mrinal Pal, Biochemistry, West Bengal University of Health Sciences, India.
(6) Yoshifumi Saisho, Keio University, Japan.
Complete Peer review History: http://sciencedomain.org/review-history/9791

Original Research Article

Received 6th April 2015
Accepted 1st June 2015
Published 16th June 2015

ABSTRACT

Background: Diabetes mellitus (DM) and its complications are on the increase especially in the developing countries with significant negative economic consequences on individuals, families and health systems.

**Corresponding author: Email: onamecwwide@yahoo.com;*

Objective: We, therefore compared albumin/creatinine ratio, microalbuminuria, and HbA1c among subjects of varying degree of complications with controls to ascertain if they can serve as markers of diabetic chronic complications to enhance early detection of chronic complications amongst diabetes mellitus patients in developing countries.
Methods: 109 type 2 DM subjects (47 males and 62 females) and 100 non-DM controls of the same age range (40-80 yrs) were recruited for this study. The chronic complications found were: nephropathy, retinopathy, coronary artery disease, cerebrovascular disease, peripheral vascular disease and diabetic foot. These were further classified into micro vascular complications (nephropathy and retinopathy) and macrovascular complications (Coronary Artery Disease, Cerebrovascular Disease, Peripheral Vascular Disease and diabetic foot).Out of these 109 DM subjects, 36 were without chronic complications, 37 have microvascular complications only and 36 have a combination of microvascular and macrovascular complications. HbA1c, Urine microalbumin and creatinine were analysed using standard methods.
Results: The mean levels of HbA1c, Microalbuminuria and albumin-creatinine ratio were significantly higher in DM subjects when compared to the control *($p<0.05$*). Microalbumin, albumin-creatinine ratio, and HbA1c were significantly higher in DM subjects with chronic complications than those without complications (*$p<0.05$*). However, DM subjects with both macro and micro complications had significant higher level of urine microalbumin, albumin-creatinine ratio, and HbA1c than those with microvascular complications only *($p<0.05$*). Subjects aged 40-45 years had significant *($p<0.01$)* albumin/creatinine ratio than subjects aged 51-55yrs as well as those >60 years. The male subjects had a significant ($p<0.01$) albumin/creatinine ratio and microalbumin respectively on comparing to their female counterpart
Conclusion: Albumin-creatinine ratio is a simple, and less cumbersome tool which could serve as a predictor of complications in type 2 diabetes mellitus.

Keywords: Type 2 diabetes mellitus; microvascular complication; macrovascular complication; microalbuminuria; urine albumin-creatinine ratio.

1. INTRODUCTION

Chronic complications of diabetes mellitus impose significant threat to individuals, families, health systems and countries' economy [1]. The threat is growing, the number of people, families and countries affected are increasing. This growing threat is an under-appreciated cause of poverty which hinders the economic development of many countries [1]. 382 million people worldwide, or 8.3% of adults, are estimated to have diabetes mellitus. About 80% live in low- and middle-income countries [2]. The WHO suggests that Nigeria has the greatest number of people living with diabetes in Africa, with an estimated burden of about 1.7 million which will increase to 4.8 million by 2030. The economic burden of diabetes is enormous in terms of the direct cost of intensive monitoring and control of blood glucose and managing cardiovascular consequences [3,4,5].

Increased Urinary protein excretion may be an early clinical manifestation of diabetic nephropathy [6], which is the main cause of high morbidity and mortality in patients with type 2 diabetes mellitus [7]. The presence of microalbuminuria precedes the development of diabetic nephropathy by 10-14 years. It is at this stage that one hopes to reverse diabetic nephropathy or prevent its progression [8]. Microalbuminuria is characterized by increased prevalence of arterial hypertension, proliferative retinopathy and peripheral neuropathy. Abnormal levels of urinary albumin occur in 30-40% of patients with type 2 diabetes and the presence of kidney disease enhances the mortality from cardiovascular disease [9]. Microalbuminuria,is an early marker of diabetic nephropathy and an independent risk factor for cardiovascular disease. The increased levels of urinary albumin secretion may represent a more generalized vascular damage than renal microvascular injury alone [9].

The albumin-to-creatinine ratio (ACR) in a single timed urinary specimen is a reflection of Urinary Albumin Excretion (UAE) and is increasingly being accepted as a marker that predicts several important health outcomes, including hypertension, kidney failure, cardiovascular events, and mortality [10,11]. The Albumin-Creatinine Ratio is also closely linked to cardio metabolic risk factors, vascular disease and insulin resistance [12].

Thus, this work will assist in emphasizing the need for regular monitoring of microalbuminuria as a preventive measure for chronic complications among diabetes mellitus patients.

2. MATERIALS AND METHODS

2.1 Study Design and Population

This is a comparative cross-sectional descriptive study designed to investigate the levels of urine microalbumin, creatinine, albumin-creatinine ratio and HbA1c levels in type 2 DM subjects with or without complication and non-diabetic controls. This study was conducted from March to May 2013 at Federal Medical Centre which lies in the heart of the metropolitan town of Makurdi, Benue State, Nigeria. The study design was approved by the Ethics Committee of Federal Medical Centre Makurdi, Benue State.

A total of two hundred and nine (209) subjects were recruited for this study. One hundred and nine (109) type 2 DM patients (36 subjects with no complications, 37 subjects with microvascular complications only and 36 subjects with a combination of micro vascular and macrovascular complications) were recruited by consecutive sampling method from diabetic clinics of Federal Medical Centre Makurdi, Benue State. Age and sex matched healthy controls were recruited from the blood bank donors as well as non- diabetic subjects.

Male and female DM patients under treatment between 40-80 yrs were included in the study. Pregnant women, non- diabetic patients, patients with proteinuria, hypoproteinemia, abnormal liver or kidney function and those treated with drugs affecting urinary albumin excretion (ACE inhibitors, angiotensin converting enzyme blocker) in the last 3 months were excluded from the study. Subjects that were diabetic, pregnant, had any form of chronic disease or less than or greater than 40-80 respectively were excluded from the control subjects.

2.2 Sample Collection and Biochemical Analysis

Early morning urine sample were collected for microalbuminuria and creatinine while whole blood sample were used for HBA1c. HbA1c was determined using device by Bio-Rad HbA1c based on Boronate affinity chromatography described by [13]. Values<7% was considered normal. Estimation of microalbumin was done using turbilatex method [14]. A diagnosis of microalbuminuria was made when the ratio of urinary albumin to creatinine ratio is > 2.0 in male and > 2.8 in women in two out of three readings. Subjects with urine albumin between 30-299mg/l in their early morning urine sample on three occasions were regarded to have microalbuminuria. Creatinine was estimated using modified jaffe's method [15].

Microalbuminuria and urinary creatinine were analyzed by Erba Mannheim, chem. 5.v3 semi automated machine.

2.3 Statistical Analysis

Data analysis was done using the statistical package for social sciences (SPSS) for windows version 20.Comparison was made using student *t-test* and ANOVA. Level of significance was taken at $p<0.05$.

3. RESULTS

The total number of subjects enrolled were 109, 17(45.9%), 10(27.8%) and 20(55.6%) of subjects with microvascular, microvascular and macrovascular complication and nil complications respectively were male while 20(54.1%), 26(72.2%) and 16(44.4%) of subjects with microvascular, microvascular and macrovascular complication and nil complications respectively were female. Microalbuminuria, urine creatinine, albumin-creatinine ratio and HbA1c is significant at $p<0.01$ on comparing diabetic subjects with control in Table 1 while Table 2 shows that subjects with microvascular complications had higher Albumin: creatinine ratio when compared with subjects without complications but subjects with both microvascular and macrovascular complications had higher albumin: creatinine ratio than those without complications as well as those with microvascular disease. Table 3 shows that there is significant $P<0.05$ correlation between albumin- Creatinine ratio and HbA1c. The age distribution of mean albumin-creatinine ratio, microalbumin, urine creatinine and HbA1c in subjects with chronic complications was depicted in Table 4, subjects aged 40-45 years had significant $(p<0.01)$ albumin/creatinine ratio than subjects aged 51-55 yrs as well as those >60 years. Table 5 shows the sex distribution of albumin-creatinine ratio, microalbumin, urine creatinine and HbA1c in subjects with chronic complications. The male subjects had a significant ($p<0.01$) albumin/ creatinine ratio and microalbumin respectively on comparing to their female counterpart.

Table 1. Urine microalbumin, creatinine, albumin creatinine ratio and glycated hemoglobin among diabetes mellitus type 2 subjects and control (Mean±SD)

Parameters	Diabetic subjects (N=109)	Control (N=100)	P-value
Micro albuminuria (mg/L)	37.97±5.90	11.15±1.00	0.000**
Urine creatinine (mmol/L)	12.25±2.74	6.4±1.75	0.000**
Albumin creatinine ratio (mg/mmol)	4.58±1.20	1.85±0.29	0.002**
HbA1c (%)	9.41±2.68	5.00±0.55	0.000**

Table 2. Urine Microalbumin, creatinine, albumin/creatinine ratio of diabetic subjects with varying complications

Parameters	No complications	Microvascular complication	Both microvascular and macrovascular complication	*P*-value
Microalbuminuria (mg/l)	33.60±8.92	37.54±8.17[a,c]	42.99±9.84[a,b]	.002
Urine creatinine (mmol/l)	14.37±4.85	13.11±7.04	9.57±6.4[a]	.022
Albumin/creatinine ratio (mg/mmol)	2.36±2.03	3.86±4.52[a,c]	7.60±4.67[a,b]	.024

a = significant at p <0.05 when compared with those with no complication. b =significant at p < 0.05 when compared with those with microvascular complication. c = significant at p < 0.05 when compared with those micro and macrovascular complication

Table 3. Pearson correlations of Microalbuminuria and Albumin creatinine ratio with Glycated haemoglobin (HbA1c)

Parameter	R	P-value
HbA1c vs Microalbuminuria	.014	.887
HbA1c vs albumin/creatinine ratio	.199*	.038

**Correlation is significant at 0.05 level. r = Correlation. P = P-value*

Table 4. Age distribution of albumin-creatinine ratio, microalbumin, urine creatinine and HBA1c in subjects with chronic complications (MEAN ± SD)

Parameters	40-45 years (n=6)	46-50 years (n=6)	51-55 years (n=13)	56-60 years (n=21)	>60 years (n=22)	P-value
Albumin-creatinine ratio	12.33±3.41[a,b,c]	3.43±1.46	2.66±0.50	6.52±2.90	2.59±0.49	.000**
Microalbumin	59.84±9.07	31.32±10.01	26.58±5.08	56.94±11.92	24.44±4.56	.001**
Urine creatinine	9.41±3.47	12.01±2.27	12.87±2.36	12.70±3.15	11.79±2.16	.726
HBA1c	9.89±2.11	10.73±3.01	8.78±2.53	10.05±2.49	8.94±2.57	.118

*a=significant when 40-45years is compared to 46-45 yrs; b=significant when 40-45years is compared to 51-55 yrs; c=significant when 40-45years is compared to >60 yrs; Values are expressed as mean ±SD.** Significant at P < 0.01; n=no of subjects*

Table 5. Sex distribution of albumin-creatinine ratio, microalbumin, urine creatinine and HBA1c in subjects with chronic complications (MEAN ± SD)

Parameters	Male	Female	P-value
Albumin-creatinine ratio	8.10±2.10	3.46±1.12	.000**
Urine microalbumin	52.24±6.67	32.32±2.35	.000**
Urine creatinine	13.79±3.86	11.03±2.93	.137
HBA1c	10.26±2.58	9.19±2.76	.824

*Values are expressed as mean + SD.** Significant at P < 0.01*

4. DISCUSSION

Diabetes mellitus is a chronic degenerative disease and poses major challenges to public health. Various biochemical changes and indices of complications have been associated with type 2 diabetes mellitus and have served as predictors of chronic complications in these patients. In this study, Microalbuminuria and albumin-creatinine ratio were significantly different from the control ($p<0.01$). This is consistent with finding by Kundu [16]. Microalbuminuria is an early marker of diabetic nephropathy and also an independent risk factor for cardiovascular disease [9]. The increased levels of urinary albumin excretion may represent a more generalized vascular damage than renal microvascular [9] injury alone. Impaired glyceamic control assessed by $HbA1_C$ is associated with increase in renal damage. Higher levels of $HbA1_C$ were associated with increased risk for development of angiopathy in the subjects. This may be due to the fact that $HbA1_C$ has special affinity for Oxygen thereby causing tissue anoxia and plays a role in causation of micro and macroangiopathy. This may damage podocyte of glomerulus leading to altered Glomerular Filteration Rate. Studies have shown a correlation between microalbumuria and $HbA1_C$ [16]. Thus, this study suggests that the diabetic subjects having poor glycaemic control are more prone to renal damage. Urine creatinine in the control was found to be significantly lower than in diabetics ($p<0.01$). Most of the control subjects were blood donors and may have drank a lot of water and food drinks as part of their preparation for blood donation while the diabetic subjects were fasting during sampling which could have led to the variation in the concentration of urine creatinine between the two subjects. Subjects aged 40-45 years had significant *($p<0.01$)* albumin/creatinine ratio than subjects aged 51-55yrs as well as those >60 years may be attributed to a poorer metabolic control in younger diabetics than in older diabetics who may have had more experience with glyceamic control. The male subjects had a significant ($p<0.01$) albumin/ creatinine ratio and microalbumin respectively on comparing to their female counterpart despite having increased urine creatinine than female. This finding is in agreement with a study done by Varghese [17]. It may be because females are mostly dependent in this part of the world hence may be given more attention by their relatives than a male counterpart.

Albumin-Creatinine ratio is elevated in subjects with both microvascular and macrovascular complications compared with those without complications. This may suggest that microalbuminuria is a marker of generalized cardiovascular disease which is consistent with findings by Battis et al. [9], thus microalbuminuria may represent a more generalized vascular damage than renal microvascular injury alone.

5. CONCLUSION

Microalbuminuria and albumin-creatinine ratio are deranged in most diabetic subjects and tend to worsen with increasing vascular complications. Therefore, they may serve as markers of chronic complications in diabetic mellitus thus may be useful in screening diabetic mellitus patients for chronic cardiovascular complications.

6. RECOMMENDATIONS

Albumin- creatinine ratio is a cheap, simple, and less cumbersome tool which may serve as a good marker/predictor of cardiovascular disease in diabetes mellitus. Because of the great public health need for a simple and inexpensive test to identify diabetic individuals at high risk of developing chronic complications, we suggest that the ACR might serve this purpose. Therefore, we advocate that it may be incorporated as a routine investigation in disease management in Nigeria to help curb or ameliorate chronic complications among diabetes mellitus patients.

7. LIMITATIONS

Larger group study should be done to verify this finding.

ETHICAL APPROVAL AND CONSENT

We hereby declare that this study was examined and approved by the Medical Ethics Committee of Federal Medical Centre Makurdi, Benue State and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed consent was obtained from all patients that participated in the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. WHO. World Health Organization consultation 5-7 November 2007. Available:http:/www.who.int/countries/nga/area/hiv/en/index.html (Accessed on 5th February 2013)
2. IDF. DIABETES ATLAS 2013 '6th edition; Available:http://www.idf.org/sites/default/files/EN_6E_Atlas_Full_0.pdf (Accessed on 8th march 2015)
3. The improved Diabetes Atlas. 3 rd ed. International Diabetes Federation; 2006.
4. Wild S, Roglic C, Green A, Sicrete R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27:1047-53.
5. Zimmet P. The burden of Type 2 Diabetes: Are we doing enough? Diabetes Metab. 2003;29:659-81.
6. Sacks G, Arnol M, Bakris G. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Diabetes Care. 2011; 34:61-68.
7. Passa P. Diabetes trends in Europe. Diabetes Metab Res Rev. 2002;3:3-8.
8. Chowta N, Pant N, Chowta M. Microalbuminuria in diabetes mellitus: Association with age, sex, weight and creatinine clearance. Indian. J Nephol. 2009;19 (2):53-56.
9. Battisti W, Palmsano J, Keane WE. Dyslipidemia in patients with type 2 diabetes: Relationships between lipids, kidney disease and cardiovascular disease. Clin Chem Lab Med. 2003;41: 1174-1181.
10. Gertsain H, Man T, Zinman B. Albuminuria and risk of Cardiovascular events, death and heart failure in diabetic individuals: JAMA. 2001;286:421-426.
11. Brantsma H, Bakker S, de Zeeuw D. Urinary albumin excretion as a predictor of the development of hypertension in the general population. J Am Soc Nephrol. 2006;17:331-335.
12. Palaniappan L, Carnethon M, Fortmann S. Association between microalbuminuria and the metabolic syndrome: NHA NES III. Am J Hypertens. 2003;16:952-958.
13. Mallia AK. Preparation and use of a boronic acid affinity support for separation and quantitation of glycosylated hemoglobins. Anal Lett. 1981;14:649-661.
14. Medcalf E, Newman D, Gorman E. Rapid, robust method for measuring low concentrations of albumin urine. Clin Chem. 1990;36(3):446-449.
15. Allen L, Michalko K, Coons C. More on cephalosporin interference with creatinine determinations. Clin Chem. 1982;28(3): 555-556.
16. Kundu D, Roy A, Mandal T. Relation of Microalbuminuria to glycosylated hemoglobin and duration of type 2 diabetes. Nigerian Journal of Clinical Practice. 2013;16 (2):216-220.
17. Varghese A, Deepa R, Rema M. Prevalence of microallbuminuria in type 2 diabetes mellitus at a diabetes centre in south India. Postgrad Med J. 2001;77: 399-402.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/9791