British Journal of Medicine & Medical Research
4(2): 766-775, 2014

SCIENCEDOMAIN *international*
www.sciencedomain.org

Relationship between Glycated Haemoglobin, Fasting Plasma Glucose, Packed Cell Volume and Albumin Creatinine Ratio in Diabetic Patients in South-South Nigeria

C. L. Sakpa[1] and J. O. Idemudia[2*]

[1]Department of Anatomy, College of Medicine, University of Benin, Benin City, Nigeria.
[2]Department of Chemical Pathology, college of Medicine, University of Benin, Benin City, Nigeria

Authors' contributions

There were equal contributions by all the authors to this manuscript. All the authors read and approved the final manuscript.

Original Research Article

Received 3rd May 2013
Accepted 10th September 2013
Published 19th October 2013

ABSTRACT

The relationship between glycated haemoglobin, fasting plasma glucose, packed cell volume and albumin creatinine ratio in diabetic patients in south-south Nigeria was investigated in 118 diabetic patients (80 females and 38 males) and 36 apparently healthy controls (20 females and 16 males). The glycated haemoglobin (HbA1c), fasting blood glucose (FBG) and albumin creatinine ratio (ACR) of (6.5±0.65%, 113±7.9mgldL and 48.4±6.3 respectively) were significantly higher in the diabetic patients than in control subjects (3.7±0.13%, 86±2.6mgldL and 21.0±5.1 respectively), while the packed cell volume (PCV) was higher in the control subjects than in diabetic patients (46.3±1.13% vs 40.6±0.92%). There was a significant positive correlation between the HbA1c, and FBG in both the diabetic patients and control subjects (r=0.418 and 0.782 respectively, P<0.001) and there was also a significant positive correlation between the HbA1c and ACR in both the diabetic patients and control subjects (r= 0.244 and 0.618 respectively, P< 0.001).

**Corresponding author: Email: osagiep2001@yahoo.com;*

In conclusion, there is a strong relationship between HbA1c, FBG and ACR in diabetic patients and control subjects.

Keywords: Diabetes mellitus; glycated haemoglobin; fasting blood glucose; packed cell volume; albumin creatinine ratio.

1. INTRODUCTION

Diabetes mellitus (DM) is a catabolic multisystem disease with both biochemical and anatomical consequences. It is a chronic disease of carbohydrate, fat and protein metabolism caused by either absolute lack of insulin or insulin resistance or secretory defects [1]. It constitutes a significant health and socioeconomic burden for patients and the health care system. According to world health organization(WHO),there were 150 million diabetic patients worldwide by the year 2000, with a projection of 221 million in 2010 and approximately 300million in 2025 [2]. India, China and the United States of America are expected to be the most affected; however the impact will be significant in developing countries where the majority of diabetic patients in 2025 will be between 45-64 years of age, which are the most productive working years [2]. The prevalence of diabetes in Nigeria varies from 0.65% in rural Mangu village to 11.0% in Urban Lagos [3].

Two commonly tested markers for monitoring diabetes mellitus are glucose level and glycated haemoglobin (HbA1c). The blood glucose test measures the level of glucose in the patients' blood at the time the sample is obtained. As such, this test provides useful, although limited information on the diabetic patients' glycaemic control. Glycated haemoglobin (HbA1c) is an important marker for long term assessment of glycaemic state in patients with diabetes. Studies show a direct relationship between HbA1c and risk for development and progression of vascular complications [4].

Goals for therapy are set at specific HbA1c target values of less than 7% [5]. HbA1c is formed by non enzymatic glycation of the N-terminal valine of the β-chain of haemoglobin in red blood cells and amount of glycated haemoglobin is directly related to the average level of glucose in the blood [6]. As blood glucose concentration rise over time, the level of glycated haemoglobin rises proportionally since circulating erythrocytes have an average half life of 60-90days, HbA1c can indicate glycaemic control over a period of 2-3months. While 4-6% of the haemogloin is glycated in non-diabetes, uncontrolled diabetes may exhibit levels in excess of 15% [7].

Diabetes is the most common single cause of end stage renal disease (ESRD) in the United States and Europe [8]. In the U.S., diabetic nephropathy accounts for about 40% of new cases of ESRD [9].The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels (30mg/day or 20ug/min) of albumin in urine, referred to as microalbuminuria. The easiest and preferred method for screening for microalbuminuria is the measurement of albumin creatinine ratio (ACR) [10]. In this study, we looked at the relationship between HbA1c, fasting plasma glucose, packed cell volume and albumin creatinine ratio in diabetic patients in south – south Nigeria.

2. PATIENTS AND METHOD

2.1 STUDY POPULATION

This study was carried out in the Departments of Chemical Pathology and Internal Medicine, University of Benin Teaching Hospital, Benin City, Edo state, Nigeria. Informed consent was obtained from the patients and the tests were performed at no cost to the patients. A total of 154 participants were recruited for this study between November 2011 and April 2012 (6 months), 118 of the participants were diabetic volunteers while 36 of them non-diabetic controls. Over 95% of the diabetic patients had type 2 diabetes mellitus and had been attending the diabetes clinic for a minimum of 12 months. Subjects with chronic medical conditions like hypertension, renal failure, liver disease and urinary tract infection were excluded from the study. All the participants were Nigerians mainly from the south-south zone. The study was approved by the ethics committee of University of Benin Teaching Hospital, Benin City, Nigeria.

2.2 SAMPLE COLLECTION

Subjects/volunteers were identified and fasted overnight. Blood samples were collected in the morning on or about 8.00am from a large vein in the cubita fossa using a 10ml syringe and dispensed into three different specimen bottles containing fluoride oxalate (for glucose estimation), Ethylene diamine tetra-acetic acid (EDTA) (for glycated haemoglobin and packed cell volume estimation) and a spot urine sample was also collected into a sterile universal bottle for urine albumin and creatinine estimation since this is more convenient for the patients than a timed (24hours, 4hours or overnight) urine collection. The blood samples were immediately centrifuged at 1257.8xg for 15minutes to separate plasma from the cells. The plasma was aspirated and stored at -20^0C until analysis was carried out for the different assays, usually within one week. Urine was assayed immediately for albumin and creatinine.

2.3 BIOCHEMICAL ASSAY

The glycated haemoglobin was estimated using the fast ion exchange separation method [11]. while the fasting blood glucose was estimated using the oxidase method [12]. The haematocit was estimated using the haematocit reader. The urine creatinine estimation was done using the modified Jaffe's method [13] and the urine albumin estimation was done using lowry method [14]. Quality control for the assays was done using randox bovine precision multisera control levels 1 and 3(lot. No. 324SE cat. No. SE1086) for each batch of assay.

2.4 DATA ANALYSIS

Data analysis was conducted using the general linear model of SAS (Statistical analysis for agric and sciences) 2004 model.

All results were expressed as mean± standard error of mean. Multiple group comparism was performed by one way ANOVA followed by Duncan test.

Pearson correlation coefficient was employed to ascertain the association between various parameters.

Chi-square test with one degree of freedom (for dichotomous variables) and unpaired t-test (for continuous variables) were used for the evaluation of differences between groups.

3. RESULTS

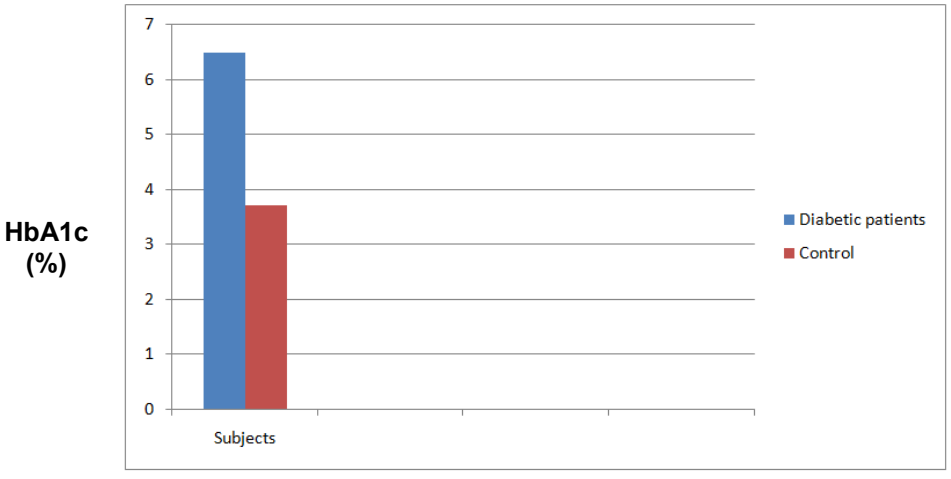
The demographic data of healthy controls and diabetic patients are stated in Table 1. The diabetic patients had significantly (P<0.05) higher values of glycated haemoglobin (HbA1c), fasting blood glucose (FBG), albumin creatinine ratio (ACR) and systolic blood pressure when compared to the healthy controls. Also the diabetic patients had higher body mass index (BMI) and diastolic blood pressure but lower packed cell volume (PCV).

Table 1. Demographic profiles of the healthy controls and diabetic patients

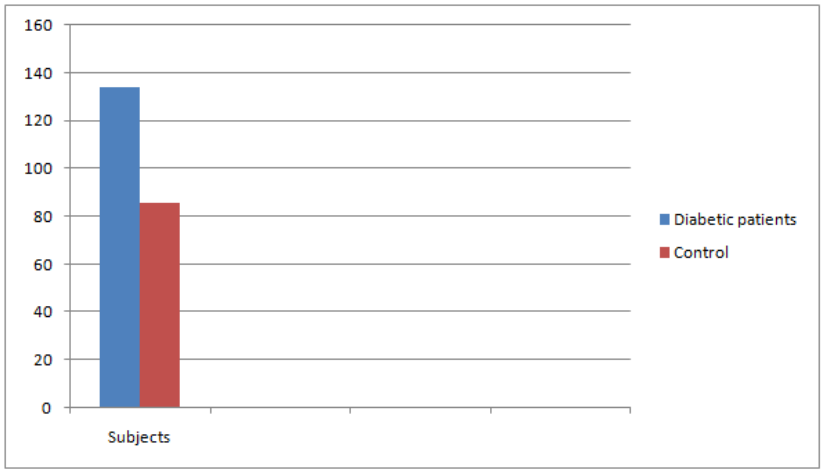
DEMOGRAPHY	CONTROL SUBJECTS N=36	DIABETIC PATIENTS N=118	P-VALUE
Gender (male/female)	16/20	38/80	0.048
Age(years)	45.26±12.723	55.80±10.503	0.605
SBP(mmHg)	117.22±18.405	135.85±22.170	0.005
DBP(mmHg)	75.0±10.617	83.48±11.457	0.214
BMI(kg/m^2)	23.07±4.319	26.55±4.667	0.04
FBG (mg/dL)	86±11.048	134±16.988	0.001
HbA1c (%)	3.72±0.568	6.50±1.917	0.022
ACR	21±2.161	48.4±3.996	0.022
PCV (%)	46.29±4.804	40.6±4.132	0.463

Note: Data were expressed as mean ± SD SBP= Systolic blood pressure, DBP =diastolic blood pressure, BMI = body mass index, FBG = fasting blood glucose, HbA1c = glycated haemoglobin, ACR = albumin creatinine ratio and PCV = packed cell volume.

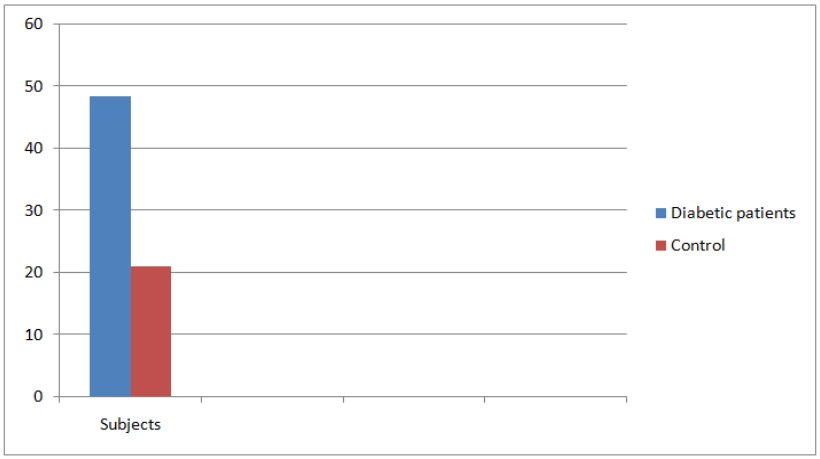
The measured biochemical parameters in the healthy control subjects and diabetic patients are presented in bar-charts in Fig. 1. This further showed the significant difference between the values of these biochemical parameters in the control subjects and diabetic patients.



HbA1c


FBG (mg/dL)
160
140
120
100
80
60
40
20
0
Subjects
Diabetic patients
Control

FBG


ACR
60
50
40
30
20
10
0
Subjects
Diabetic patients
Control

ACR

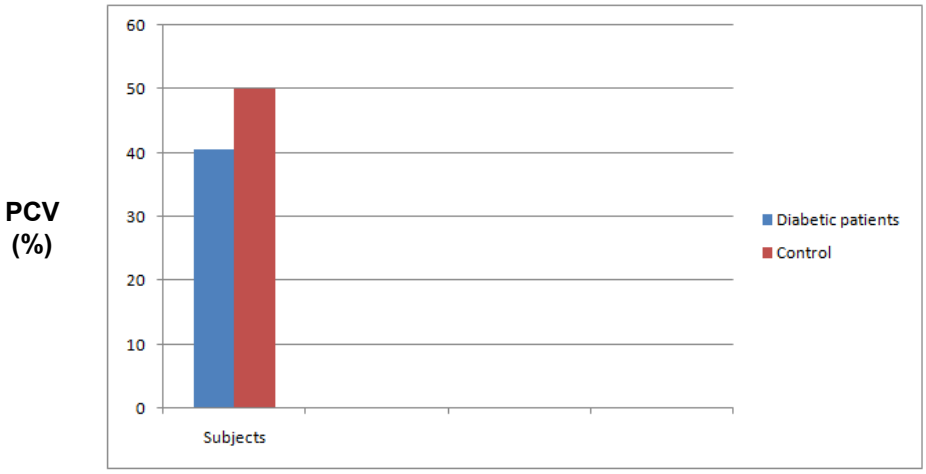


Fig. 1. Showing the measured biochemical parameters in the diabetic patients and healthy control subjects.

The correlation results shown in this study (Table 2, Fig. 2. and 3) between fasting blood glucose and glycated haemoglobin, glycated haemoglobin and albumin creatinine ratio were very strong (correlation coefficient >0.5).

Table 2. Correlation between the parameters in controls and diabetic patients

CONTROLS	HbA1c	FBG	ACR	PCV
HbA1c	1.000	0.782	0.528	0.061
FBG	0.782	1.000	0.323	0.060
ACR	0.528	0.323	1.000	0.123
PCV	0.061	0.060	0.123	1.000
DIABETICS				
HbA1c	1.000	0.418	0.244	0.418
FBG	0.418	1.000	0.268	0.617
ACR	0.244	0.268	1.000	0.110
PCV	0.418	0.617	0.110	1.000

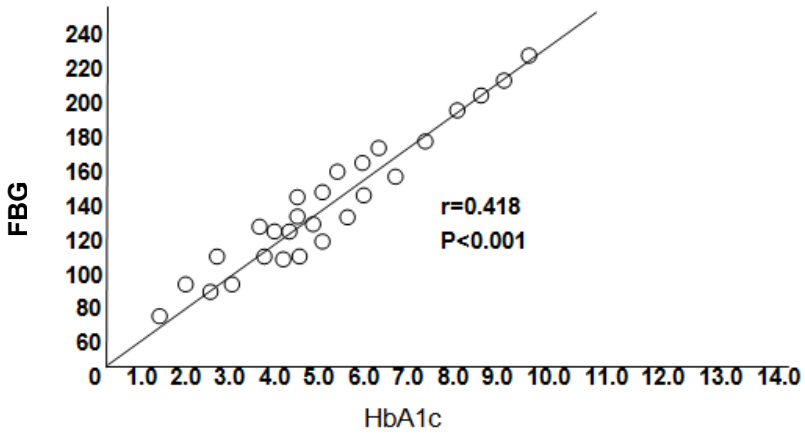


Fig. 2. Graph showing agreement between FBG and HbA1c

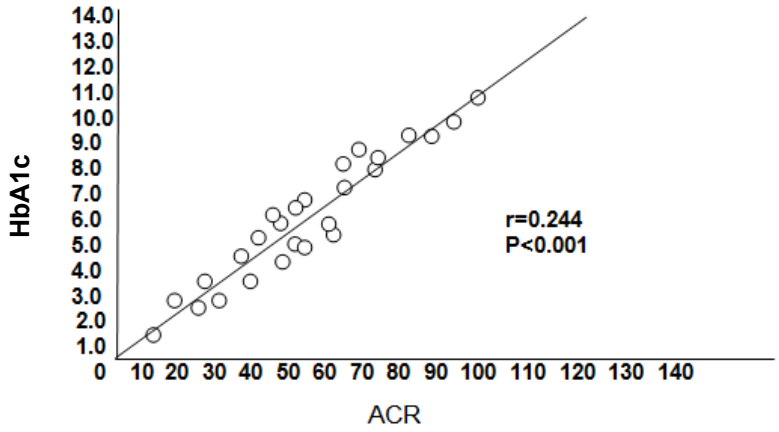


Fig. 3. Graph showing agreement between HbA1c and ACR

4. DISCUSSION

The mean age of the diabetic patients in this study was 55.28 years, this is low compared to reports from developed countries where most diabetic patients were over 64 years of age[15], but similar to observations from other sub-sahara African countries where an age range of 45 – 64 years was reported [15,16].

.

In most parts of developing countries the only means of screening for diabetes or monitoring its treatment is by determination of fasting plasma glucose concentration [17]. The role and importance of glycated haemoglobin in the long term assessment of diabetic patients has been recognized and appreciated [18].

In this study, the mean HbA1c and FBG levels did not meet the target goals in the diabetic patients; this is in agreement with a previous study from Nigeria which documented poor glycaemic control among diabetic patients[19].

The reasons for poor glycaemic control among Nigerian diabetic patients are multifactorial. Financial constrain is a key factor as most patients have to pay out of pocket for their drugs and for blood glucose tests, and at a price which has been found to be much higher than the cost of these drugs in other parts of the world [20]. The WHO report estimated that 90.2% of Nigerians live below the poverty level of $2 per day, thus, accessing health care is a challenge for people living with diabetes in Nigeria [21]. This difficulty is evident by reports showing a high prevalence of complications due to diabetes [22,23].

This study also demonstrated a good agreement between these two parameters (HbA1c and FBG) in the assessment of glucose metabolism in diabetes. There was a significant positive correlation between glycated haemoglobin and fasting plasma glucose in both the diabetic patients and control subjects ($r=0.418$ and 0.782 respectively, $P<0.001$). This indicated that the higher the fasting plasma glucose, the higher the glycated haemoglobin and this implies that glycosylation of haemoglobin increases with increase in plasma glucose concentration[12]. Despite the fact that the relationship between HbA1c, FBG and PCV in control and diabetic subjects has not been established, in this study, we found a higher packed cell volume in controls than the diabetic patients. This is in agreement with a previous study done by Akinloye et al in South West Nigeria, they demonstrated that the effect of gender and packed cell volume on glucose metabolism is lost in diabetic patients and they concluded that FBG and HbA1c are therefore the sole indicator of glucose metabolism in diabetic patients [24].
.
The albumin creatinine ratio is a marker for the degree of glomerular damage which could be used as a diagnostic tool for diabetic nephropathy. It serves as a sensitive early indicator of the adverse effect of diabetes mellitus on the kidney and it is a powerful predictor of the subsequent course of diabetic nephropathy [25,26]. The finding of a positive correlation between glycosylated haemoglobin (HbA1c) and albumin creatinine ratio (ACR) suggests that poor glycaemic control is associated with progression of microalbuminuria; this is in agreement with the findings of Erasmus et al in South Africa [27]. This was further emphasized by the microalbuminuria collaborative study of the United Kingdom group which found correlating HbA1c concentration with the development and progression of microalbuminuria and overt nephropathy in their study [28].

CONCLUSION

We have demonstrated in this present study that there is a strong relationship between HbA1c, FBG and ACR in diabetic patients. HbA1c and FBG are the main parameters used in monitoring glucose metabolism in diabetic patients in South South Nigeria and ACR can be used to screen diabetic patients at risk of developing diabetic nephropathy

ACKNOWLEDGEMENT

We wish to thank Mr. Momoh Anthony of the department of Chemical Pathology, University of Benin Teaching Hospital, Benin City, Nigeria for typing the manuscript.

CONSENT

All the participants were properly briefed about the study and an informed consent was obtained from them before venous blood was collected.

ETHICAL APPROVAL

The study was approved by the Ethics committee of the University of Benin Teaching Hospital, Benin City, Nigeria.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Crook AM. Clinical chemistry and metabolic medicine. Edward Arnold, UK, 7th edu. 2006;Pp 182-183
2. Global Burden of Diabetes, World health organization press release WHO/63 (Geneva: September 14, 1998. 2010. available on www.who.int/inf-pr1998/en/pr98-63.html
3. Akinkugbe OO, final Report of National Survey on Non-communicable Diseases in Nigeria Series 1. Federal Ministry of Health and Social Services, Lagos;1997.
4. The diabetes control and complication trial research group. The effect of intensive treatment of diabetes on the development and progression of long-term complication in insulin-dependent diabetes mellitus. N. Engl J. Med. 1993;329:977-986
5. American diabetes association. Standard of medical care in diabetes-2007, diabetes care 2007;30:S4-S4.1
6. ADA Position statement: Standards of medical care in diabetes-2007.. Diabetes care 30, supplement 1. 2007;S32- S41
7. Goldstein DE, Little RR, Lorenz R.A, Malone JI. Tests of glycaemia in diabetes. Diabetes care 2004;27(7):1761-1773
8. American Diabetes Association. Hypertension management in adults with diabetes (position statement). Diabetes care 2004;27 suppl 1:S65S567.
9. Bakris GL, Williams M, Dworkin L, Elliot WJ, Epstein M et al. Preserving renal function in adults with hypertension and diabetes: a consensus approach. AMJ kid Dis 2000; 646-661.
10. Mogensem CE, keane WF, Bennelt PH, Jerums G, Parving H-H, et al. Prevention of diabetic renal disease with special reference to microalbuminuria. Lancet 1995; 346:1080-1084.
11. Peacock I. Glycosylated haemoglobin measurement and clinical use. J clin pathology 1984; 37(8):841-851.
12. Barham D and Trinder P. An improved colour reagent for the determination of blood glucose by the oxidase system. Analyst 1972; 97,142-145.
13. Tietz N.W. clinical guide to laboratory test; W.B. Saunders company Philadelphia, USA 2nd edn,1990:554-556.
14. Llowry OH, Rosebraugh HJ, Farr AL, Randall RJ. Determination of microalbuminuria in diabetic patients. J Biol chem. 195;193-265

15. 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;27:1047-1053.
16. McMichael AJ, Beaglehole R. The changing Global Concept of Public Health. Lancet 2000;356:495-499.
17. Dandson MB, Schriger DL: Relationship between fasting plasma glucose and glycosylated haemoglobin. Journal of the American Medical Association 1999; 281(13):1203-1210.
18. Malik M, Gill GV, Heynigden CV, Pugh RN. Assay methods for glycated haemoglobin: A review for tropical hospitals. International Diabetes Digest, 1996:7, No. 1 Jan.
19. Rotimi CN, Chem G, Oli J, Ofogbu E, Okafor G, Acheampong J, et al. Calpain-10 Gene polymorphisms and Type 2 Diabetes in West Africans; The Africa America Diabetes mellitus (A ADM) stud. Ann Epidemiol 2005;15:153-159.
20. WHO 2004 Diabetes Action Now Booklet. Geneva, Switzerland; World Health Organization; 2004. Available from http: // www: who. Int /diabetes/ booklet.
21. Ofoegbu EN. Cardiac Autonomic Neuropathy in Nigeria Type 2 Diabetes mellitus patients. Global J Med Sci 2005;4:52-58.
22. Richard WG, Paul AP, James BM, Daniel ES. Trends in the Complexity of Diabetes care in the United States from 1991 to 2000. Arch Intern Med 2004; 164:1134-9.
23. Amercian Diabetes Association. Management of Dyslipidaemia in Adults with Diabetes. (Position statement). Diabetes care 2002; 25 suppl 1:S574-S577.
24. Akinloye O.A, Adaramoye O.A, Akinlade K.S, Odetola A.A, Raji A.A. Relationship between fasting plasma glucose and glycated haemoglobin in adult diabetic Nigerians. Afr J Biomed Res 2007;10:127-132
25. Dilandro D, Catalano C, Lambertini D, Bordin V, Fabbian F, et al. The effect of metabolic control on development and progression of diabetic nephropathy. Nephrol Dial Transplant. 1998;13(suppl. 8):35-43.
26. Foggensteiner L, Mulroy S, Firth J. Management of diabetic nephropathy J.R Med 2001;94:210-217.Soc.
27. Microalbuminuria collaborative study group, UK. Risk factors for development of Microalbuminuriain insulin dependent diabetic patients: a cohort study. BMJ 1993:306,1235-1239
28. Erasmus RT, Blanco EV, Okesina AB, Mesa J. Hypertension, proteinuria and renal insufficiency in black South Africans with non-insulin dependent diabetes. Diab. Int. 1999;9:57-58.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=298&id=12&aid=2294