Research Article

Glycated Albumin as a Prognostic Marker in Diabetic Nephropathy

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Abstract

Background: Diabetic nephropathy is a global health concern and it is the most common etiology of end-stage kidney disease, strict glycaemic control reduces the development and progression of diabetes-related complications. Markers of long-term glycemic control are essential tools in the care of diabetic patients. The objective of this study is to investigate the correlations between glycated albumin concentration which is a tool of glycemic control, and different stages of diabetic nephropathy. **Methods:** This is a prospective case control study included a total of 90 participants who were classified into 4 groups according to urinary albumin excretion as: *Group (I) (Control):* includes 15 healthy control, *group (II): (Normoalbuminuria):* includes 25 patients with urinary albumin excretion < 30 mg/gm Cr., *group (III): (Microalbuminuria)*: includes 25 patients with urinary albumin excretion from 30 to 300 mg/gm Cr and *group (IV): (Macroalbuminuria, group):* includes 25 patients with UAE > 300 mg/gm Cr. From all subjects, complete history was taken and they were subjected to full examinations and some laboratory investigations including (renal and liver functions, lipid profile, HbA1c, glycated albumin, etc..). Also, abdominal ultrasonography and Fundus Examination were in done. **Results:** The results showed that there was a significant increase in AST, cholesterol, triglycerides, LDL, urea, creatinine, A/C ratio, fasting and random blood sugar and HBA1c and glycated albumin values with increasing degree of albuminuria, while, albumin and HDL had taken the opposite trend. There was a significant positive correlation between Glycated albumin and age, BMI, FBG, RBG, HBA1C, Cholesterol, LDL ($P<0.01$) and with HDL, ALT, AST ($P=0.04$), albumin ($P=0.03$), however, Glycated albumin level was not affected significantly by HTN, IHD or stroke. ROC curve results of serum Glycated Albumin as a marker of diabetic nephropathy showed that the optimal cutoff was ≤14.47 and area under curve (AUC) was 0.99 %, with a highly significant P. value, sensitivity was 98.1% and specificity was 94.4%. **Conclusion:** Glycated albumin can be used as an indicator for assessing short term glycemic control in type 2 diabetic subjects with different degree of renal impairment but not with massive albuminuria. Also, glycated albumin is directly proportional with HbA1c and provides short term glycemic control due to rapid albumin turnover (2-3weeks). In addition, the results revealed that macroalbuminuria patients have a higher incidence of micro and macrovascular complications.

Keywords: Glycated Albumin, Prognosis, Marker, Diabetic Nephropathy.

Introduction

Diabetic nephropathy (DN) is defined as albuminuria (albumin excretion rate > 300 mg/24 h) and declining renal function in a patient with known diabetes in the absence of urinary tract infection or any other renal disease, it is a public health concern of increasing proportions and reasons for a significant reduction in life expectancy of diabetic patients (Aldukhaye, 2017). It is the most common etiology of end-stage kidney disease (ESKD), strict glycaemic control reduces the development and progression of diabetes-related complications, and there is evidence that improved metabolic control improves outcomes in diabetic subjects with advanced chronic kidney disease (CKD) (Frederiek et al., 2011). About of 20-40% of type 2 diabetic patients with microalbuminuria (MA) progress to manifested nephropathy after 20 years from the onset of diabetes; approximately 20% develop end-stage renal disease (Gaede et al., 2008).

Markers of long-term glycemic control are essential tools in the care of diabetic patients,

currently, measurement of HbA1c is the most commonly used and best evaluated marker for both glycemic control and prediction of vascular complications (ADA, 2012). However, HbA1c measurements are affected by variant hemoglobin (Hb) and some diseases that shorten the lifespan of erythrocytes such as hemolytic anemia and renal anemia (Goldstein et al, 2004).

Glycated albumin (GA) may represent a better marker of glycemic control than HbA1c indiabetic patients (Peacock et al., 2008). Glycation is the bonding of a sugar molecule, such as glucose, to a lipid or protein molecule, such as albumin, thus, glycated albumin refers to albumin to which glucose has bonded . Albumin is present not only in blood, but also in major organs and body fluids (Vos et al., 2011). Albumin serves to maintain cell shape and plays an important function in the distribution of hormones, nutrients and some drugs in the body (Hasslacher et al., 2014). It was reported that the amount of glycated albumin decreases when blood glucose levels are low and increases when blood glucose levels are high (Koga and Kasayama, 2010).

Glycated albumin is not influenced by the above mentioned factors which affect HbA1c concentrations but instead reflects glycemic control over a shorter period of time (2-3 weeks) due to the much shorterhalf-life of albumin (Hasslacher et al., 2014).Additionally, Glycated proteins influences renal function and thus alter the permeability properties of the glomerular capillary wall and are preferentially transported across the glomerular filtration barrier into the mesangial space (Daniels and Hauser, 1992). Earlier work suggests preferential tubule cell uptake of the gly-cated forms of protein which have adverse effect on renal microvasculature (Viswanathan et al., 2009).

The objective of this study is to investigate the correlations between glycated albumin concentration which is a tool of glycemic control, and different stages of diabetic nephropathy.

Subjects and Methods

This is a prospective case control hospital based study which recruiting four groups of individuals attending at Internal Medicine department of Minia University Hospital between September 2016 to April 2017. A total of 90 participants were included in this study (15 healthy control subjects and 75 diabetic patients) and were classified into 4 groups according to urinary albumin excretion (UAE) level as follow:

Group (I) (Control group): includes 15 healthy control subjects to evaluate and compare the data of patients who already had diabetes with either normo, micro, macroalbuminuria.

Group (II): (Normoalbuminuria group): includes 25 patients with urinary albumin excretion less than 30 mg/g of creatinine (mg/gm Cr).

Group (III): (Microalbuminuria, group): Includes 25 patients with urinary albumin excretion from 30 to 300 mg/gm Cr.

Group (IV): (Macroalbuminuria, group): Includes 25 patients with UAE more than 300 mg/gm Cr.

We excluded from this study all patients of type 1 diabetes mellitus, patients with obstructive uropathy, patient with inflammatory condition, any patient taking medications such as steroids or non-steroidalanti-inflammatory and patient with HCV+ve AB& HBs Ag +ve.

All patients and controls were subjected to the following:

1. Thorough complete history taking
3. Laboratory Investigations
2. Thorough clinical examination
4. Radiological Investigation
5. Fundus Examination

Results

Table (1): Demographic and clinical presentations in studied groups:

Variable		Groups				P. value (Sig.)
		Group (I) Control	Group (II) Normo	Group (III) Micro	Group (IV) Macro	
Age (year)		25.3 ± 5.7	54.2 ± 9.2	54.9 ± 8.1	56.8 ± 9.4	**0.00****
Sex	**Male**	4 (16.0%)	4 (16.0%)	6 (24.0%)	13 (52.0%)	**0.03***
	Female	21 (84.0%)	21 (84.0%)	19 (76.0%)	12 (48.0%)	
Smoking		2 (13.3%)	3 (12.0%)	2 (8.0%)	4 (16.0%)	0.86^{NS}
Alcohol		0	2 (8.0%)	0	1 (4.0%)	0.38^{NS}
BMI		22.5^{b} ± 3.4	26.2^{a} ± 4.1	23.5^{b} ± 2.7	26.4^{a} ± 4.8	**0.00****
Diabetes		0	25 (100.0%)	25 (100.0%)	25 (100.0%)	**0.00****
Duration of DM (yr)	**1:5**	-	6 (24.0%)	8 (32.0%)	3 (12.0%)	0.17^{NS}
	> 5:10	-	18 (72.0%)	14 (56.0%)	14 (56.0%)	
	> 10:15	-	1 (4.0%)	3 (12.0%)	5 (20.0%)	
	> 15:20	-	0	0	2 (8.0%)	
	> 25	-	0	0	1 (4.0%)	
Medication of DM	**Oral**	-	15 (60.0%)	15 (60.0%)	8 (32.0%)	0.16^{NS}
	Insulin	-	10 (40.0%)	10 (40.0%)	16 (64.0%)	
	Both	-	0	0	1 (4.0%)	
HTN		0	3 (12.0%)	2 (8.0%)	7 (28.0%)	**0.04***
IHD		0	2 (8.0%)	5 (20.0%)	6 (24.0%)	0.119^{NS}
Stroke		0	0	3 (12.0%)	4 (16.0%)	0.096^{NS}
Systolic BP		112.7 ± 8.8	113.6 ± 13.8	112.4 ± 14.2	120.8 ± 19.6	0.182^{NS}
Diastolic BP		72.7 ± 4.5	72.8 ± 8.4	72.0 ± 7.6	77.2 ± 11.0	$0.13.1^{NS}$

a, b, c Means in the same row with different superscript are significantly different.

Table (2): Laboratory characteristics of studied groups.

Variable	Groups				P. value (Sig.)
	Group (I) Control	Group (II) Normo	Group (III) Micro	Group (IV) Macro	
ALT (U/L)	21.5 ± 5.2	26.9 ± 12.9	25.7 ± 11.4	28.3 ± 17.2	0.439^{NS}
AST (U/L)	20.5^{b} ± 5.4	27.6^{ab} ± 11.4	30.3^{ab} ± 13.3	31.2^{a} ± 12.2	**0.00****
Albumin (g/dL)	4.55^{a} ± 0.19	4.39^{b} ± 0.24	4.29^{b} ± 0.22	3.85^{c} ± 0.43	**0.00****
Cholesterol (mg/dL)	138.8^{c} ± 39.1	183.9^{b} ± 46.3	198.6^{ab} ± 60.6	219.2^{a} ± 48.5	**0.00****
Triglycerides (mg/dL)	110.9^{b} ± 39.4	127.5^{ab} ± 24.9	138.1^{ab} ± 61.2	156.7^{a} ± 81.8	**0.04***
LDL (mg/dL)	76.3^{c} ± 26.4	103.9^{b} ± 37.6	124.9^{ab} ± 40.2	146.2^{a} ± 23.1	**0.008****
HDL (mg/dL)	40.3 ± 3.3	39.7 ± 5.5	38.4 ± 6.4	37.7 ± 6.1	0.419^{NS}
Urea (mg/dL)	27.7^{c} ± 4.7	31.7^{c} ± 11.4	45.8^{b} ± 17.1	74.1^{a} ± 33.3	**0.00****
Creatinine (mg/dL)	0.61^{c} ± 0.14	0.73^{c} ± 0.38	1.23^{b} ± 0.72	2.49^{a} ± 1.16	**0.00****
GFR	129.9^{a} ± 10.2	96.3^{b} ± 25.7	65.6^{c} ± 25.5	29.9^{d} ± 17.9	**0.00****
A/C ratio	0.001^{b} ±0.009	0.007^{b} ±0.003	0.10^{b} ± 0.06	3.32^{a} ± 2.19	**0.00****
Fasting BG	77.7^{b} ± 10.2	157.5^{a} ± 52.2	165.8^{a} ± 65.6	175.6^{a} ± 63.5	**0.00****
Random BG	105.1^{b} ± 11.9	233.6^{a} ± 74.1	258.2^{a} ± 84.7	268.9^{a} ± 67.6	**0.00****
HbA1C	3.31^{b} ± 0.55	8.45^{a} ± 2.13	9.41^{a} ± 2.38	8.26^{a} ± 2.41	**0.00****
Glycated Albumin	12.84^{c} ± 1.01	20.30^{b} ± 3.63	26.03^{a} ± 3.52	20.97^{b} ± 1.84	**0.00****

a, b, c Means in the same row with different superscript are significantly different.

Table (4): Optimal cutoff, AUC, P.Value, Sensitivity & Specificity of Serum Glycated Albumin.

	Optimal cutoff	AUC	P. value	Sensitivity	Specificity
Glycated Albumin	**≤14.47**	**0.991**	**<0.001****	**98.1**	**94.4**

Table (3): Correlations between Glycated Albumin and other variables.

Correlations		*Correlation coefficient (r)*	P. value (Sig.)
Glycated Albumin	*** age**	0.62	**0.00****
	*** BMI**	0.28	**0.00****
	*** Urea**	0.14	0.17^{NS}
	*** Creat.**	0.15	0.18^{NS}
	*** FBG**	0.52	**0.00****
	*** RBG**	0.63	**0.00****
	*** HbA1C**	0.82	**0.00****
	*** A/C ratio**	-0.02	0.85^{NS}
	*** Cholesterol**	0.39	**0.00****
	*** TG**	0.15	0.16^{NS}
	*** LDL**	0.37	**0.00****
	*** HDL**	-0.27	**0.04***
	*** AST**	0.21	**0.04***
	*** ALT**	0.22	**0.04***
	*** Albumin**	-0.24	**0.03***

Table (5): Clinical and Laboratory characteristics of the studied groups as per KDOQI guidelines.

Variable	eGFR Groups				P. v. (Sig.)
	eGFR ≥90 (ml/min) (n=23)	eGFR 60-89 (ml/min) (n=13)	eGFR 30-59 (ml/min) (n=22)	eGFR ≤ 30 (ml/min) (n=17)	
M/F	5:18	3:10	8:14	7:10	0.48
Age (year)	52.3 ± 7.6	52.7 ± 7.8	57.6 ± 9.5	58.4 ± 9.1	0.07^{NS}
HTN	2 (8.7%)	1 (7.7%)	3 (13.6%)	6 (35.3%)	0.09^{NS}
IHD	1 (4.3%)	1 (7.7%)	5 (22.7%)	6 (35.3%)	0.06^{NS}
Stroke	1 (4.3%)	1 (7.7%)	3 (13.6%)	2 (11.8%)	0.72^{NS}
Alcohol	3 (13.0%)	0	0	0	0.07^{NS}
HbA1C	8.82^{ab} ± 2.71	9.63^{a} ± 1.91	8.85^{ab} ± 2.51	7.66^{b} ± 1.46	**0.04***
Urea (mg/dL)	31.09^{c} ± 9.3	41.00^{c} ± 20.2	48.95^{b} ± 16.1	86.18^{a} ± 31.9	**0.00****
Creat. (mg/dL)	0.57^{c} ± 0.13	0.94^{c} ± 0.18	1.49^{b} ± 0.31	3.12^{a} ± 1.08	**0.00****
Glycated Alb.	20.9^{b} ± 4.7	25.7^{a} ± 3.5	23.0^{b} ± 3.2	21.8^{b} ± 2.8	**0.00****

Discussion

Table (1) shows baseline demographic and clinical data of the studied groups. There was a female predominance with a significant change in age among groups (p=0.03), also, there was a significant increase between groups in BMI where group II, IV were the highest groups with a statistical significant difference between all groups and between them and group III, I. Also, there was a significant difference in between groups as regard prevalence of hypertension (p=0.04).

Results of table (2) show that there was no significant change between groups as regard

ALT values, but there was significant statistical increase in AST, albumin, cholesterol, triglycerides, LDL, urea, creatinine, A/C ratio, fasting and random blood sugar and HBA1c, glycated albumin values (P<0.01) except for Triglycerides and LDL (P<0.048,0.008 respectively) where group IV was the highest among all groups except in albumin values where group I was the highest and in glycated albumin where group III was the highest.

As regard Albumin concentration, there was a significant decrease in group IV versus control group (p<0.05) with a significant difference between all groups (p<0.01). As regard cholesterol there was a significant elevation in between group IV and group II but no significant change between any of them and group III .As regard Triglyceride, there no significant change between IV and neither group II nor group III but there was a significant elevation in group IV versus control group (p=0.048). As regard LDL there was a significant change between group IV and both group I,II but no difference between group III and neither group II nor group IV. Regarding urea and creatinine concentrations, there was a significant difference between group IV and group III and between group III and group II. There was a significant difference between group IV and the other Three groups in A/C ratio. As regard fasting, random blood sugar and HBA1C there was statistical differences in between the three studied groups and the control group. As regard GA, there was a significant differences between group III versus group IV, group III versus group I.

The results shows that regarding abdominal ultrasound and fundus changes, there were no significant statistical differences in between groups, there were 2 patients in group IV with fatty liver, one patient in group II and group III had fatty liver with mild splenomegaly. As regard fundus examination, there were 10 patients with diabetic retinopathy in group IV and one patient in group III , Also there was two patients with corneal opacity in group IV, one patient in group III, only one patient had a myopic fundi in group II. There was a significant statistical difference in between groups (p<0.01).

Table (3) show correlation between Glycated Albumin and other variables. There was a significant positive correlation between Glycated albumin and age, BMI, FBG, RBG, HBA1C, Cholesterol, LDL (P<0.01) and with HDL, ALT, AST (P=0.04), albumin (P=0.03). The results show that there was no significant statistical difference between patients who had HTN, IHD or Stroke and those who did not have any of them regarding Glycated Albumin level.

Table (4) presents the optimal cutoff of ≤14.47 and area under curve (AUC) of 0.99%, with a highly significant P. value, sensitivity of 98.1% and specificity of 94.4 0f serum Glycated Albumin as a marker of diabetic nephropathy (fig. 1).

Results of table (5) show clinical and laboratory characteristics of the studied groups per KDOQI guidelines which show prevalence of females than males in all groups .There was a significant elevation in level of Glycated Albumin in patient with eGFR (60-89) versus the other three groups(p<0.01)There was a significant statistical difference in level of HBA1c(P=0.04) at which patients with eGFR (60-89) had significant higher level of HBA1c versus patients with eGFR(≤30) (p<0.01).There was no significant statistical difference in prevalence of stroke, IHD ,HTN in between groups.

Conclusion

In summary, our results revealed that glycated albumin can be used as an indicator for assessing short term glycemic control in type 2 diabetic subjects with different degree of renal impairment but not with massive albuminuria. Also, glycated albumin is directly proportional with HbA1c and provides short term glycemic control due to rapid albumin turnover (2-3weeks). In addition, the results revealed that Macroalbuminuric patients have a higher incidence of micro and macrovascular complications.

References

1. Abd Elgyoum A.M, H. Osman et al., (Ultrasonography Patterns for Diabetic Nephropathy according to the Body

Shape), Scholars Journal of Applied Medical Sciences (SJAMS) 2014; 2(5C): 1649-1652
2. ADA, (2012): American Diabetes Association. Standards of medical care in diabetes. Diabetes Care, 2012; 35 Suppl 1:S11-63.
3. Aldukhaye Abdulrhman . Prevalence of diabetic nephropathy among Type 2 diabetic patients in some of the Arab countries. Int J Health Sci (Qassim). 2017 Jan-Mar; 11(1): 1–4.
4. Brownlee M, Aiello LP, Cooper ME, Vinik AI, Plutzky J, Boulton AJM.Complications of diabetes mellitus.Williams Textbook of Endocrinology. 13th ed. Philadelphia, PA: Elsevier Saunders; 2016:chap 33.
5. Daniels BS & Hauser EB. Glycation of albumin, not glomerular basement membrane alters permeability in an in vitro model. Diabetes, 1992;41:1415-1421.
6. David R. Jacobs, Jr.,Maureen A. Murtaugh, Michael Steffes,Xinhua Yu, Jeffrey Roseman, and Frederick C. Goetz1.American Journal of epidemiology, 2002;155(12):1114-119.
7. de Boer IH, Sibley SD, Kestenbaum B, et al., Central obesity, incident microalbuminuria, and change in creatinine clearance in the epidemiology of diabetes interventions and complications study. J Am Soc Nephrol. 2007 Jan;18(1):235-43.
8. Diercks GF, Stroes ES &Van Boven AJ. Difference in the relation between urinary albumin excretion and carotid intima-media thickness in nondiabetic and type 2 diabetic subjects. Diabetes Care, 2002; 25:936–937.
9. Dinu I., Moţa E. Glycated albumin – more than the missing link in the evaluation of diabetes control. Rom J Diabetes Nutr Metab Dis. 2014, 21(2):137-150
10. Don BR & Kaysen G.Serum albumin: relationship to inflammation and nutrition. Semin Dial, 2004; 17: 432–437.
11. Frederiek E. Vos, John B. Schollum, and Robert J. Walker. Glycated albumin is the preferred marker for assessing glycaemic control in advanced chronic kidney disease. NDT Plus. 2011 Dec; 4(6): 368–375.
12. Freedman BI, Shenoy RN & Planer JA. Comparison of glycated albumin and hemoglobin A1c concentrations in diabetic subjects on peritoneal and hemodialysis. Perit Dial Int, 2010; 30: 72–79.
13. Gaede P, Lund-Andersen H, Parving HH, et al., Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med. 2008;358:580–591.
14. Gerchman Fernando , Jenny Tong, et al., Body Mass Index Is Associated with Increased Creatinine Clearance by a Mechanism Independent of Body Fat Distribution. J Clin Endocrinol Metab. 2009 Oct; 94(10): 3781–3788.
15. Gerstein HC, Miller ME, Byington RP.Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008; 358: 2545–2559
16. Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan D, Peterson CM and Sacks DB. Tests of glycaemia in diabetes. Diabetes Care, 2004; 27:1761-1773.
17. Haraldsson B, Nystrom J&Deen WM. Properties of the glomerular barrier and mechanisms of proteinuria. Physiol Rev, 2008;88: 451–487.
18. Hasslacher C, Kulozik F, Platten I and Lorenzo Bermejo J. Glycated albumin and HbA1c as predictors of mortality and vascular complications in type 2 diabetes patients with normal and moderately impaired renal function: 5-year results from a 380 patient cohort. J Diab Res Clin Met, 2014; 3:9.
19. Ikizler TA, Pupim LB &Brouillette JR. Hemodialysis stimulates muscle and whole body protein loss and alters substrate oxidation. Am J PhysiolEndocrinolMetab, 2002; 282: E107–E116.
20. Kobayashi Hiroki , Masanori Abe, Yoshinori Yoshida, Hiroko Suzuki, Noriaki Maruyama, and Kazuyoshi Okada. Glycated Albumin versus Glycated Hemoglobin as a Glycemic Indicator in Diabetic Patients on Peritoneal Dialysis. Int J Mol Sci. 2016 May; 17(5): 619.
21. Koga M and Kasayama S. Clinical impact of glycated albumin as another glycemic control marker. Endocr J. 2010; 57:751-62
22. Kondaveeti SB, D K, Mishra S, Kumar R A and Shaker IA.Evaluation of glycated albumin and microalbuminuria as early risk markers of nephropathy in type 2 diabetes mellitus. J Clin Diagn Res, 2013 Jul;7(7):1280-1300.

23. Miedema K.Standardization of HbA1c and Optimal Range of Monitoring". Scandinavi an Journalof Clinical and Laboratory Inves tigation, 2005: 61–72.
24. Mo Y, Ma X, Li H, Ran X, Yang W, Li Q, Peng Y, Li Y, Gao X, Luan X, Wang W, Xie Y & Zhou J.US National Library Of Medicine, 2016;115:17-23.
25. Okada T, Nakao T, Matsumoto H, Nagaoka Y, Tomaru R, Iwasawa H & Wada T. Influence of proteinuria on glycated albumin values in diabetic patients with chronic kidney disease. Intern Med, 2011;50:23–29.
26. Okada T, Nakao T, Matsumoto H, Nagaoka Y, Tomaru R, Iwasawa H & Wada T. Influence of proteinuria on glycated albumin values in diabetic patients with chronic kidney disease. Intern Med, 2011;50:23–29.
27. Padmaja K Rani, Rajiv Raman, Aditi Gupta, Swakshyar S Pal, Vaitheeswaran Kulothungan and Tarun Sharma. Diabetology & Metabolic Syndrome, 2011; 3:9.
28. Peacock TP, Shihabi ZK, Bleyer AJ, Dolbare EL, Byers JR, Knovich MA, Calles-Escandon J, Russell GB and Freedman BI. Comparison of glycated albumin and hemoglobin A1C levels in diabetic subjects on hemodialysis. Kidney Int. 2008; 73:1062-8.
29. Peacock TP, Shihabi ZK, Bleyer AJ, et al., Comparison of glycated albumin and hemoglobin A1C levels in diabetic subjects on hemodialysis. Kidney Int. 2008; 73:1062-8.
30. Piga, R., Y. Naito, S. Kokura, O. Handa, and T &Yoshikawa. Short-term high glucose exposure induces monocyte-endothelial cells adhesion and transmigration by increasing VCAM-1 and MCP-1 expression in human aortic endothelial cells, 2007; 193: 328–334.
31. Richard J. G..US National Library Of Medicine, 2010; 12(5): 364–368.
32. Schleicher ED, Olgemoller B & Wiedenmann E. Specific glycation of albumin depends on its half-life. Clin Chem, 1993; 39: 625–628.
33. Stevens LA, Coresh J, Schmid CH, Feldman et al., Estimating GFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD.Am J Kidney Dis, 2008; 51:395-406.
34. Viswanathan Vijay, Satyavani Kumpatla, Priyanka Tilak, Parthiban Muthukumara. Levels of glycated albumin at different stages of diabetic nephropathy in India. Int J Diabetes & Metabolism (2009)17:77-80 77
35. Vos Frederiek E. , John B. Schollum, and Robert J. Walker. Glycated albumin is the preferred marker for assessing glycaemic control in advanced chronic kidney disease. NDT Plus. 2011 Dec; 4(6): 368–375.
36. W. Russo LM, Sandoval RM & Campos SB.Impaired tubular uptake explains album inuria in earlydiabetic nephropathy. J Am Soc Nephrol, 2009;20(3):489-94.
37. Wright CM, Parker I, Lamont D &Craft Aw.Amplications of childhood obesity for adult health. Findings of thousands families for Cohort studies. BMJ, 2001; 323;1280-1284.