Role of HbA1c and microalbuminuria in diabetic-hypertensive individuals: An index for the diabetic nephropathy

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Received: 24th September, 2018 **Accepted:** 1st November, 2018

Abstract

Introduction: The present study was carried out to assess the influence of advanced glycosylation end products, microalbuminuria, and hypertension in development of nephropathy in diabetic-hypertensive individuals. Microalbuminuria has been shown to be a risk factor for nephropathy in patients with type 2 diabetes with uncontrolled glycemic index. In this study, we aimed to explore the association advanced glycosylated end products between microalbuminuria and other risk factors in the development of diabetic nephropathy in diabetic-hypertensive individuals.

Materials and Methods: A total of 131 individuals were randomly recruited in the study and were segregated into three groups. Group-1 is normal (n=50) and group-II contains control DM (n=22) and group-III contains uncontrolled DM (n=59). Medical records were used to collect data of age, SBP, DBP and history of diabetes, hypertension. Blood samples were collected to estimate FBS, PPBS, glycosylated hemoglobin (HbA1C), and urine for estimation the urinary albumin.

Result: The FBS, PPBS, SBP has shown a significant rise between the controls and uncontrolled diabetes, where as DBP has show significant rise in the controlled diabetes in caparison to control group. Microalbuminuria and HbA1c has shown a significant rise in control diabetes and uncontrolled diabetes group when compared with control group. Microalbuminuria has shown a significant correlation with SBP, FBS, PPBS and HbA1c. ROC analysis indicates HbA1c and microalbuminuria are good markers for diabetic nephropathy.

Conclusion: Increased levels of microalbuminuria and advanced glycosylated end products will increase the compliance of diabetic-hypertensive individuals for developing the nephropathy.

Keywords: Diabetes, Glycated hemoglobin, Microalbuminuria.

Introduction

With epidemiological, demographic, lifestyle and nutrition transition, non-communicable diseases like DM, HTN are increasing in India. Diabetic patients in developing countries like India are even more vulnerable to develop the microvascular complications of diabetes, including diabetic nephropathy and that too at an early age of life.[1]

Studies of Roberto Pedrinelli et al[2] says that, high blood pressure when transmitted to renal glomeruli, it might increase the glomerular ultrafiltration of albumin. Hypertension may increase capillary pressure and acute elevation in systemic perfusion pressure may accelerate hyperfiltration. The transcapillary macromolecular transport and might damage each of several different pathways, such as diffusion through endothelial cell membranes, passage via intercellular junctions, transendothelial channels of organs and tissues with highly different permeability, as well the surface area products, which alters systemic capillary permeability in essential hypertension.[3]

Microalbuminuria is considered to be an early stage of diabetic nephropathy, which is the leading cause of end stage renal disease worldwide.[4,5] It is the primary sign of renal predicting overt nephropathy.[6] Hence urine albumin is used as a very sensitive prognostic marker explicit nephropathy in patients with diabetes.[7] Monitoring levels of microalbuminuria and other risk factors associated with this condition will makes an importance in preventing or postpone overt nephropathy.[1]

In this present study, we aimed to explore the association of advanced glycosylation end products (HbA1c) between microalbuminuria in diabetic-hypertensive individuals in the development of diabetic nephropathy.

Materials and Methods

The study was carried out with the patients attending to the out patients departments for health check up's at Apollo speciality Hospital, Nellore. A total of 131 individuals were randomly recruited in the study and were segregated into three groups. Group-1 is Normal (n=50) and group-II contains control DM (n=22) and group-III contains uncontrolled DM (n=59). Informed consent were obtained from the individuals. Study was cleared by the institutional ethical clearance. Medical records were used to collect data like age, SBP, DBP and history of diabetes, hypertension. Blood samples were collected after 12 hours overnight fasting to analyze FBS, PPBS, using fully automated chemistry analyzer (Iris Diuri-400) whereas urinary albumin, HbA1C are estimated using immunoturbidometric kit method (DiaLab). Statistical work was done using SPPS-20.0 software. p value was considered significant at ≤0.05 level.

Results

The FBS, PPBS, SBP has shown a significant rise between the controls and uncontrolled diabetes, where as DBP has shown significant rise in the controlled diabetes in caparison to control group. Microalbuminuria and HbA1c has

shown a significant rise in control diabetes and uncontrolled diabetes group when compared with control group (Table 1). HbA1c has shown a significant correlation with SBP, DBP, FBS, PPBS and Microalbuminuria with r values 0.744, 0.231, 0.708, 0.810 respectively. Microalbumin has shown a significant correlation with FBS, PPBS and HbA1c, SBP with r values 0.211, 0.333, 0.398, 0.197 respectively (Table 2). ROC analysis indicates HbA1c and Microalbuminuria are good markers for diabetic hypertension with area under curve values (1.0, 0.680) with cut-off values (9.45, 429) respectively (Table 3).

Table 1: Comparison of different parameters between the control and study groups

Variable(s)		Normal (n=50) Group-I	Control DM (n=22) Group-II	Uncontrolled DM (n=59) Group-III	Significance Between Normal and study group
Age (years)		49.3±9.6	55.33±15.1	53.11±11.8	NS
Gender	Males	30	12	40	--
	Females	20	10	19	
Microalb mg/lit		16.04±4.1	121.82±50.6	131.75±65.1	Sig Group II & III
FBS mg/dl		91.35±8.29	109.92±18.08	156.26±58.0	Sig Group III
PPBS mg/dl		126.28±10.03	152.09±41.52	240.14±60.21	Sig Group III
HbA1c %		5.10±0.27	6.90±1.40	7.89±1.03	Sig Group II & III
SBP mmHg		122.02±8.95	124.82±11.7	151.08±18.2	Sig Group III
DBP mmHg		79.18±24.4	68.96±26.5	82.01±19.8	Sig Group II

Note: p value was considered significant at <0.05.

Table 2: Correlation between different parameters

Variable(s)	Micro Albumin	HbA1c
Age	0.94	0.189*
Microalb	1	0.398**
FBS	0.211*	0.708**
PPBS	0.333**	0.810**
HbA1c	0.398**	1
SBP	0.197*	0.744**
DBP	0.115	0.231**

Note: * significance at 0.05 level; ** significance at 0.01 level.

Table 3: ROC curve analysis

Test variable(s)	Sensitivity	Specificity	Area Under Curve	Asymptotic 95% Confidence Interval		Cut-off Value
				Lower Bound	Upper bound	
Microalb mg/lit	0.051	0.972	0.647	0.680	0.855	429
HbA1c %	0.085	1.000	1.000	1.000	1.000	9.45

Discussion

Significant rise in the FBS and PPBS levels in conjunction with microalbuminuria and HbA1c in both study groups indicates the formation of the AGE products, which will be the risk factor for the development of secondary complication in the diabetes. The significant rise of the SBP and micro albumin in both study groups indicates the future risk for the development of the nephropathy.[8]

Microalbuminuria an early sensitive marker in life of the altered cardio metabolic milieu that is associated with susceptibility in individual with CV disease in prediabetes and prehypertension. It is therefore an ideal target for early-primary prevention using CV-protective therapy regimens.[9] Albuminuria shown to be closely associated with salt intake as well as blood pressure.[10]

In our correlation study between the microalbuminuria and SBP has shown a significant correlation, which signifies the role of hypertension in diabetes influencing the glomerular ultrafiltration of albumin. In general, mainly SBP and to a lesser extent pulse pressure, is a major determinant for albuminuria. In fact, albuminuria remains almost unaltered with SBP within the normal range. In contrast, the response of the left ventricle to SBP is linear within the whole range of SBP. Some factors such as, use oral contraception in women and impaired glucose tolerance were shown to influence microalbuminuria.[11] Studies of Cohen MP et al, has found some other factors that impinge on glomerular permeability by modifying cytokines and affecting permeability. Increased amounts of glycated albumin reduce glomerular nephrin and increase vascular endothelial growth factor.[12] In addition to above factors, increase sodium intake

and intraglomerular pressure, high protein intake other wisely, poorly controlled blood pressure increase glomerular permeability in diabetes and, hence, micro albuminuria is observed.[13]

The microalbumin has also shown significant correlation with FBS, PPBS and HbA1c which shows the effect of glycemic index on glomerular membrane our study is correlated with the studies of, Ishibashi Y et al, and Tourigny A et al, reported that, albumin is glycated in individuals with diabetes, and forms advanced glycation end products, which in turn leads to production of reactive oxygen species, and other cellular toxins which will leads to vascular injury. The effect of pressor hormones, such as angiotensin-II will magnify the injury, resulting in a earlier progression of vascular injury. Which will direct the injury to the vascular smooth muscle cells, endothelial cells, and visceral epithelial cells of the glomerular capillary wall membrane as well as influencing the proximal tubular, and epithelial cells of basement membrane of nephron.[12,14,15]

Our study – HbA1c and Micro albuminuria has shown more area under curve which shows to be a good biomarkers for glycemic index and as well as glomerular capillary wall membrane permeability. Patel V et al reported that micro albuminuria may be most sensitive indicator to diagnose incipient diabetic nephropathy.[16]

Conclusion

It is clear now that both the increased glycemic index forms advanced glycation end products and generates reactive oxygen species which will leads to vascular injury and the rise in systolic blood pressure will also influence glomerular permeability by modifying cytokines production that affect permeability. So both hypertension and uncontrolled blood sugar levels influence the development of nephropathy.

Acknowledgements: Nil.

Conflict of Interest: None.

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How to cite this article: Srilakshmi P, Reddy RKYV, Bharathi PK, Rambabu K. Role of HbA1c and microalbuminuria in diabetic-hypertensive individuals: An index for the diabetic nephropathy. *Int J Clin Biochem Res* 2019;6(1):126-128.