ISSN - 2320-6039 (Print) ● ISSN - 2320-608X (Electronic)

Volume 4 / Number 1 / January-June 2016

INTERNATIONAL JOURNAL OF PHYSIOLOGY

Website: www.ijop.net

International Journal of Physiology

Print-ISSN: 2320-6039 Electronic-ISSN: 2320-608X Frequency: Six Monthly

Website:www.ijop.net

Editor

Dr. R.K. Sharma
Institute of Medico-legal Publications
4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110 001

Printed, published and owned by

Dr. R.K. Sharma
Institute of Medico-legal Publications
4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110 001

Published at

Institute of Medico-legal Publications
4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110 001

International Journal of Physiology

www.ijop.net

CONTENTS

Volume 4, Number 1 **January-June 2016**

DOI Number: 10.5958/2320-608X.2016.00020.2

Prevalence of Microalbuminuria - An Early Detector of Diabetic Nephropathy

Prabhavathi K[1], Kirthana Kunikullaya[2], Hemamalini R V[3], Jaisri G[4], Saravanan A[5]

[1]Associate Professor, Department of Physiology, SRM Medical College, Hospital and Research Centre, Potheri,
[2]Assistant Professor, Department of Physiology, M.S. Ramaiah Medical College, Bangalore,
[3]Associate Professor, Department of Physiology, SRM Medical College, Hospital and Research Centre, Potheri,
[4]Professor, Department of Physiology, M.S.Ramaiah Medical College, Bangalore, [5]Professor, Department of Physiology, SRM Medical College, Hospital and Research Centre, Potheri

ABSTRACT

Background: Microalbuminuria is the presence of albumin in urine above the normal level but below the detectable range of conventional methods. Its presence is an early marker of diabetic nephropathy.

Aim & Objectives: 1. Detect prevalence of microalbuminuria in type 2 diabetic patients.

2. Correlate microalbuminuria with age, sex and duration of disease.

3. Correlate microalbuminuria with blood sugar (fasting and post- prandial), serum creatinine and Blood urea nitrogen (BUN).

4. Compare microalbuminuria in controlled (HbA1c<7) and uncontrolled (HbA1c> 7) type II diabetics.

Method: Around 100 cases of diabetic patients of age group 30-80 years, with duration of diabetics more than one year were examined for fasting and postprandial blood sugar(FBS and PPBS), HbA1c, BUN and serum creatinine. Also 24 hour urine sample was analysed for microalbuminuria by turbidometric method.

Results: The prevalence of microalbuminuria was 48% with p value 0.004. Also a significant correlation of microalbuminuria was seen with FBS, PPBS, BUN, and serum creatinine. However no correlation of microalbuminuria was established with HbA1c and duration of disease. Further microalbuminuria was increased in uncontrolled diabetics than controlled diabetics though it is not statistically significant.

Conclusion: Our study concludes that microalbuminuria is essential for early detection of diabetic nephropathy. Therefore it is recommended that microalbuminuria test should be done at regular intervals for type II diabetes mellitus.

Keyword: *Type II diabetics, microalbuminuria, HbA1c, diabetic nephropathy.*

INTRODUCTION

Diabetes mellitus is a worldwide public health concern and is associated with reduced mortality and significant morbidity. It leads to specific diabetes related macro vascular complications like myocardial infarction, stroke, renal failure, blindness and amputations. According to the World Health Organization (2004), diabetes affects more than 170 million people worldwide, and this number will rise to 370 million by 2030. About one third of type 2 diabetics will eventually have progressive deterioration of renal function[1]. Microalbuminuria is an abnormal elevation of albumin levels in the urine that cannot be detected using conventional dipstick method[2]. It is defined as urinary albumin excretion between 20-200 μg/min or upto 15 mg/L over a 24 hour period[3]. It represents very early stages of diabetes mellitus (DM) when glomerular filtration rate (GFR) is normal .Thus it is an early marker of the subsequent development of proteinuria and diabetic nephropathy a leading cause of end stage renal disease and premature cause of death worldwide. Progression to established diabetic nephropathy occurs through several stages and microalbuminuria predicts future development of overt nephropathy[4].

Diabetic nephropathy occurs in about 30% of patients with type 1 diabetes mellitus & 25% of patients type 2 diabetes mellitus[5]. The purpose of this study was to evaluate the presence of microalbuminuria in patients with DM and toascertain its relationship with the age, disease duration, blood sugar levels, HbA1c, BUN and Creatinine.

MATERIAL & METHOD

This is a retrospective study carried out in 100 type 2 diabetes mellitus patients to detect the prevalence of microalbuminuria and to investigate correlation of microalbuminuria with age, sex, duration of the disease, blood sugar levels, HbA1c and markers of renal damage like BUN, serum creatinine. The study was conducted in M.S. Ramaiah Medical College and approved by institutional ethical committee board. Patients from both sexes were included. Fasting blood samples of the patients were analysed for FBS, PPBS, HbA1c, and BUN and serum creatinine. Also 24 hour urine collection was done for the analysis of microalbuminuria by turbidometric method which is considered as more sensitive assays.

1. FBS, PPBS in blood was estimated by glucose oxidase- peroxidase (GOD- POD) method.
2. Microalbumin in urine was estimated by turbidometric method.
3. Serum Creatinine was estimated by Jaffe's method.
4. BUN by colorimetric method.

STATISTICAL METHOD

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of microalbuminuria (mg/lt) between controlled (HbA1c<7) and uncontrolled (HbA1c> 7) type II diabetics. Pearson correlation has been used to find the significance of relationship between microalbuminuria and study parameters in the cases.

RESULTS

In our study the prevalence of the disease is 48% with a significant p value of 0.004 (Table 1). Also the study showed a positive correlation of microalbuminuria with FBS (p = 0.0001) and PPBS (p= 0.005) (Table 2). The study did not show significant correlation with age, disease duration and HbA1c. However a significant correlation of microalbuminuria was observed with) serum creatinine (0.0001) (Table 3) and BUN (p= 0.009 (Table 4). Further microalbuminuria was elevated in uncontrolled (HbA1c> 7) type II diabetics than controlled (HbA1c<7) diabetics but it is not statistically significant.

Table 1 - Prevalence for the Present Study

MA							
	N	**%**		**Mean**	**SD**	**Independent t Test**	**P Value**
Normal	52 [0 - 15]	52.0		7.22	3.89	2.988	0.004 **
Abnormal	48 [> 15]	48.0		426.77	1012.94		

Table 2- Relationship of FBS, PPBS with MA

Correlation between FBS and MA					
	N	**Mean**	**SD**	**Pearson Correlation [r]**	**P Value**
MA	100	208.606	729.044	0.362 [Moderate +ve Correlation]	0.0001 ***
FBSS	100	158.466	57.686		

Correlation between PPBS and MA					
	N	Mean	SD	Pearson Correlation [r]	P Value
MA	100	208.606	729.044	0.277 [Low +ve Correlation]	0.005 **
PBSS	100	233.929	81.705		

Table 3- Correlation between MA and Serum Creatinine

Correlation between Serum Creatinine and MA					
	N	Mean	SD	Pearson Correlation [r]	P Value
MA	100	208.606	729.044	0.455 [Moderate +ve Correlation]	0.0001 **

Table 4- Correlation between MA and BUN

Correlation between BUN and MA					
	N	Mean	SD	Pearson Correlation [r]	P Value
MA	100	208.606	729.044	0.261 [Low +ve Correlation]	0.009 **
BUN	100	12.759	7.305		

DISCUSSION

Diabetic nephropathy has become the most common single cause of end-stage renal disease (ESRD)all over the world[6]. The first clinical sign of renal dysfunction in patients with diabetes generally is microalbuminuria a sign of endothelial dysfunction that is not necessarily confined to the kidney. Microalbuminuria develops in 2 to 5 percent of patients of type 2 diabetes per year[7,8]. The present study assessed the prevalence of microalbuminuria in type II diabetes mellitus a strong predictor of nephropathy [9]and ESRD. As the duration of diabetes progresses in untreated patients it leads to numerous microvascular complication one of them being nephropathy. Thus diabetic nephropathy progresses gradually and accounts for about 40% of ESRD.

Most of the studies reveal that, diabetic patients do not present with well developed clinical manifestation of nephropathy[10]. However the same studies have proven significant microalbuminuria in these patients [5,11]. Thus the magnitude of damage caused by the microvascular complication of diabetes stress needs a sensitive marker for screening nephropathy. And this sensitive marker has known to be the estimation of microalbumin excretion in the urine[12,13]. According to WHO, the prevalence rate of nephropathy after 15 years of diabetes ranged between 17.7 and 56.6% in men and between 11.1 and 71% in women. Increased protein excretion may be an early clinical manifestation of diabetic nephropathy[14,15,16].In other studies the prevalence rate of microalbuminuria was 34% and 27.2% [3,17]. In our study the prevalence rate is 48% which was found to be statistically significant. However the variation in the prevalence range could be due to a difference in the patient selection criteria and different estimation technique. Further proteinuria independently associates with coronary heart disease in patients with diabetics and reflects not only renal impairment but a key pathogenic element of generalised vascular damage.Gene polymorphism of angiotensin converting enzyme has known to be associated with diabetic nephropathy[18]. Thus pathogenesis appears to involve complex interactions between genetic and environmental factors[19]. The patho-physiologic basis for elevated urinary albumin excretion entails the binding of glucose to proteins resulting in excessive protein glycosylation with the build-up of advanced glycated end products. This leads to deposition of advanced glycated end products on the glomerulus resulting in renal and glomerular hypertrophy, mesangial matrix accumulation and thickening of glomerular basement membrane. This abnormality permits the leakage of low molecular weight proteins [albumin][20]. As the diabetic nephropathy progress in early stage no clinical signs and symptoms of glomerular changes are seen. Thus the onset can be diagnosed by screening for microalbuminuria.

High sugar levels for long duration causes microvascular complication like retinal damage leading to loss of vision (retinopathy), sensory nerve damage (neuropathy) and irreversible kidney

damage (nephropathy). Since microalbuminuria is an early indicator of nephropathy, its prevalence rate was assessed in our study and was correlated with other markers of kidney damage like BUN and serum creatinine. Also in our study, microalbuminuria showed a significant positive correlation with both fasting and post prandial hyperglycaemia, which means that as the sugar levels raised the microalbumin excretion in urine also increased. This goes in accordance with previous studies [14]. In this study, no positive correlation was seen between microalbuminuria and age when compared to other studies wherein the levels were higher in older age group[3,6]. However male patients (69%) have been found to be more susceptible to microalbuminuria as compared to female patients (31%) similar to the previous studies[4]. Further no positive correlation between microalbuminuria and duration of disease was established, as compared to other studies where the levels were higher in patients with the longer duration of disease [21,22]. Also the study did not show positive correlation between microalbuminuria and HbA1c when compared to previous study [12].

Previous studies have shown a significant elevation of microalbuminuria in uncontrolled type II diabetics (HbA1c> 7) than controlled type II diabetics (HbA1c<7)[23]. However in our study the levels were higher in uncontrolled diabetics when compared to normals but it was not statistically significant.

Over the last few years, the association between microalbuminuria and cardiovascular events has been established. A strong relation of microalbuminuria, raised serum creatinine levels and presence of cardiac and vascular hypertrophy explain the excess morbidity and mortality rates observed in patients with renal dysfunction. This supports the role of the kidneys as an integrated sensor of cardiovascular risk[24]. In this study also a significant positive correlation was seen between microalbuminuria and serum creatinine in accordance with previous study[25]. Also a linear correlation between BUN levels and prevalence of microalbuminuria was observed in this study. It is interesting to note that increase in urea may increase prevalence of microalbuminuria in diabetic patients.

CONCLUSION

Our study has found a significant prevalence of microalbuminuria in type II diabetics indicating subclinical damage of microvasculature, which is the predictor of development of diabetic nephropathy. Further as Microalbuminuria showed a positive correlation with FBS, PPBS, Serum creatinine and BUN it is the marker of choice for the detection of renal involvement in patients with diabetics. Hence, it is recommended that microalbuminuria test should be a part of routine check-up forDM. Further this alerts the physician to take precautionary measures for renal damage by timely administration of treatment strategy and correction of risk factor.

Acknowledgement: We would like to express our gratitude to V.Christopher Amalraj, Assistant professor in Biostatistics, Department of Community Medicine, SRM Medical College, Hospital and Research centre, Kattankulathur, Chennai, Tamil Nadu, for helping us with the statistics for this work. The authors disclose that we did not receive any financial or writing assistance.

Conflict of Interest: The authors declare that they have no conflict of interest.

Source of Funding: Nil

REFERENCES

1. Remuzzi G, Schieppati A and Ruggenenti P (2002). Nephropathy in patients with type 2 diabetes. The New England Journal of Medicine 346 1145-51.
2. Tobe SW, McFarlane PA and Naimark, DM (2002). Microalbuminuria in diabetes Mellitus. Canadian Medical Association Journal 167 (5) 499-503.
3. Buranakitjaroen P etal J Med Assoc. Thai 2005 Nov; 88(11)16249.
4. Ahmedani MY, Hydrie MZI, Iqbal A, Gul A, Mirza WB and Basit A (2005). Prevalence of Microalbuminuria in Type 2 Diabetic Patients in Karachi: Pakistan A Multi-center Study. Journals of Pakistan Medical Association 55(9) 382-386.
5. William J Marshall et tal American diabetes Association. Diabetes care , Vole 27, Suppliment1, Jan-2004.
6. Molitch ME, DeFronzo RA, Franz MJ, Keane WF, Mogensen CE, Parving HH and Steffes MW (2004). The American Diabetes Association:

Nephropathy in diabetes (Position Statement). DiabetesCare 27(Suppl. 1) S79 –S83.

7. Gall MA, Hougaard P, Borch-Johnsen K and Parving HH (1997). Risk factors for development of incipient and overt diabetic nephropathy in patients with non-insulin dependent diabetes mellitus:prospective, observational study. BMJ 314 783-788
8. Adler AI, Stevens RJ, Manley SE, Bilous RW and Cull C (2003). Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney International 63 225-32.
9. Viberti GC, Jarrett RJ, Keen H. Microalbuminuria as prediction of nephropathy in diabetics. Lancet 1982; 2: 611
10. Bharathi R, Radhakishan N, Naveen Kumar T, Neetha K, Srilatha 627-632,Estimation Of Microalbumin In Type – 2 Diabetes Mellitus, Journal of Evolution of Medical and Dental Sciences/ Volume 3/ Issue 03/January 20, 2014
11. A.C. Buch, M. Dharmadhikari, N.K. Panicker S.S. Chandanwale and Harsh Kumar,Microalbuminuria: An Early Detector Of Diabetic And Hypertensive Nephropathy, International Journal of Basic and Applied Medical Sciences ,2012 Vol. 2 (2) May-August,pp.218-225
12. Prevalence of small vessel and large vessel disease in diabetic patients from 14 centers. The World Health Organization Multinational study of vascular disease in Diabetics. Diabetes drafting group.Diabetologia.1985:28,(Suppl) :615-40
13. Sobngwi E, Mbanya JC, Moukouri EN, Ngu KB. Microalbuminurai and Retinopathy in diabetic population of Cameroon. Diabetes Res Clin Pract. 1999;44; 191-96
14. Sacks DB, Arnold M, Bakris GL. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Diabetes care 2011 ;34-61
15. Gross JL, azevedo MJ, Silveiro SP.Diabetic nephropathy: diagnosis, prevention and treatment .Diabetes care 2005 : 28-164.
16. Ruggenti P, remuzzi G.Nephropathy of type 2 diabetes mellitus.J Am soc Nephrol1998 ;9:2157
17. Meisinger C, Heier M, Landgraf R, Happich M, Wichmann HE and Piehlmeier W (2008). Albuminuria, cardiovascular risk factors and disease management in subjects with type 2 DM: a crosssectional study. BioMed Central Health Services Research 8 226-233
18. Demaine A, Hibberd M, Millward A. Insertion/ deletion polymorphismin the angiotensin –converting enzyme gene.Diabetologia 1995;38: 1:1495-96
19. Powers A C. Diabetes Mellitus. In: Jameson JL. (editor) Harrison's Endocrinology. 1st ed. New York: McGraw-Hill;2006.303–304.
20. Mason RM, Wahab NA. Extracellular matrix metabolism in diabetic nephropathy. J Am Soc Nephrol 2003;14:1358-1373.
21. Sheikh SA, Baig JA, Iqbal T, Kazmi T, Baig M and Husain SS (2009). Prevalence of Microalbuminuria with relation to Glycemic Control in Type-2 Diabetic Patients in Karachi. Journal of Ayub Medical College, Abbottabad 21 (3) 83-86.
22. Escobedo J, Rana JS, Lombardero MS, Albert SG, Davis AM, Kennedy FP, Mooradian AD, Robertson DG, Srinivas VS, Gebhart SP and for the BARI 2D Study Group (2010). Associationbetween albuminuria and duration of DMand myocardial dysfunction and peripheral arterial disease among patients with stable coronary artery disease in the BARI 2D study. Mayo Clinic Proceedings 85(1) 41–46.
23. IranparvarAlamdariM,AminisaniN,Bashardoost B, Shamshirgaran SM, Khodamo-radzadeh M, Shokrabadi M, Olomi B (2006).Prevalence and Risk Factors of Microalbuminuria inType 2 Diabetic Patients in a Diabetic Clinic ofArdabil-Iran Int J Endocrinol Metab; 4: 8-12
24. Leoncini G, Viazzi F, Parodi D, Vettoretti S, Ratto E, Ravera M, Tomolillo C, Sette MD, Bezante GP, Deferrari G and Pontremoli R (2003). Mild Renal Dysfunction and Subclinical Cardiovascular Damage in Primary Hypertension. Hypertension 42 14-18
25. Manisha Baghel , Sudhir Modala , *BJ Pradeep Kumar and P Parimala (2014) . Correlation Of Creatinine Clearance And Urine Microalbumin In Type 2 Diabetes Mellitus. International Journal of Basic and Applied Medical Sciences Vol. 4 (2) May-August, pp. 182-186.