

Original Research Article

A prospective study on urinary microalbuminuria as surrogate marker of vascular endothelial dysfunction, in patients of ischemic stroke

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ABSTRACT

Background: Presence of overt proteinuria has been independently linked to greater stroke risk. The objectives of this study were to determine the relationship between the for ischemic stroke and albuminurea as a marker for vascular events. Microalbuminuria, is an early marker of both kidney disease and endothelial dysfunction, may be associated with global vascular risk, but the nature and relationship between microalbuminuria and incident ischemic stroke has not been clearly defined. The purpose of this study was to assess the association of microalbuminuria and ischemic stroke.

Methods: Study enrolled 150 admitted patients of acute ischemic stroke. The patients were assessed by questionnaire, microalbuminuria, creatinine clearance after detailed history taking and thorough clinical examination.

Results: The combined common risk factors were HTN (80%), diabetes (33%) and smoking (53%). The hypertensive patients had 8 times higher risk of microalbuminuria as compared to normotensive patients (95% 1.8-31.0 $p < 0.05$). Among diabetes patients had risk of microalbuminuria 30 times higher compared to euglycemic patients (95% CL 9.6-78.8 $p < 0.01$). The smoker patients had 8 times risk of microalbuminuria (CL 95%-1.2-22.8 $p < 0.16$). However, the patients who had dyslipidemia had risk of microalbuminuria 1.07 times who have normal lipid level, but it was statistically insignificant (98% CL 0.8-4.1 $p > 0.05$). The 38 patients out of 46 patients who had microalbuminuria has high normal serum creatinine with creatinine clearance (45-59 mL/min/1.73 m². (82% versus. 4.4% 30.44 mL/min/173m²). The risk of microalbuminuria was higher in patients who had high normal serum creatinine (1.4 mg/dL) with creatinine clearance of 45-59 mL/min/1.73 m² versus normal serum creatinine 0.8 mg/dL.

Conclusions: The finding of the study, show the microalbuminuria is an independent risk factor for vascular endothelial dysfunction, in patient of diabetes early renal dysfunction and HTN, extrapolating the vascular event (ischemic stroke).

Keywords: Creatinine clearance, Microalbuminuria

INTRODUCTION

Presence of overt proteinuria has been independently linked to greater stroke risk furthermore, emerging data suggest that microalbuminuria may boost stroke risk but the full extent of the relationship between urinary albumin excretion and stroke has not been established.^{1,2} Microalbuminuria is considered as a marker of vascular endothelial damage, the latter being the underlying cause

of vascular diseases microalbuminuria may be related to vascular damage by several biological pathways like renal dysfunction, transvascular escape of albumin, endothelial dysfunction and inflammation microalbuminuria as an independent risk factor for ischemic stroke has been widely published, microalbuminuria has been positively correlate with carotid-intimal thickness, a well-recognized marker of cerebrovascular disease increasing the awareness of

microalbuminuria as an early prognostic indicator of stroke risk.³⁻¹⁰

The goal of this study is designed, therefore, to determine its relationship to risk factor for stroke.

METHODS

A cross sectional observation study was carried in Department of Medicine, M. G. M. Medical College, Indore, Madhya Pradesh, India during period of April 2015-July 2016. The study was approved by Ethics Committee of M. G. M. Medical College, Indore, Madhya Pradesh, India. The study is performed on 150 patients admitted in medical I. C. U. under department of medicine.

Eligibility criteria

Ischemic stroke survivor who have at least two traditional risk factor like DM / HTN / cigarette smoking etc.

Exclusion criteria

Clinical feature similar to stroke like: subarachnoid hemorrhage, Subdural hematoma, epilepsy, previous stroke, epilepsy, T.I.A., patient with overt albuminuria (>300 mg/day), UTI, CCF, pregnant female, bed-ridden patient for more than 2 weeks, septicemia and infection. The patients were assessed by questionnaire, clinical examination, routine investigation including HbA1C, urine for microalbumin, CT / MRI brain.

Criteria for diagnosis of DM

- FBS>126 mg/dL
- HbA1C > 6.5%
- 2-hour plasma glucose 200 mg/dL after oral glucose tolerance test.

Assessment for microalbuminuria

Microalbuminuria was tested by Micral Test (Roche Diagnostic) manufacture limited. The test was dependent on color reaction and was mediated by an antibody bound enzyme. This method has shown good correlation with radioimmunoassay and can be readily used for screening. A reading more than 30 mg/dL was considered as positive.

Definition of microalbuminuria

Refer to urinary albumin excretion above 30 mg/dL and less than 300 mg/dL.

Statistical analysis

The discrete data were assessed in number and percent. Chi-square test was used for determining the relation between HTN, DM, dyslipidemia, smoking and

microalbuminuria p value (2 sided) <0.0005 represent statistical significance.

Statistical significance assessed by SPSS version 10.

Spearman-Rank non-parametric correlation was applied between study parameter.

RESULTS

A total of 150 patients of ischemic stroke (median age 55 years) who were enrolled in prospective study. The commonest age group of ischemic strokes (44%) is 51-60 years of age (Table 1).

Table 1: Age wise distribution of patients.

Age group in years	Number of patients
Up to 40	10 (6.6%)
41-50	12 (08%)
51-60	66 (44%)
61-70	36 (24%)
Above 70	26 (17%)

According to our study, we have 150 patients (mean age 55 year) diagnosed with ischemic stroke, confirmed by Computed Tomography, who were admitted to the intensive care unit within 24 hours after the onset of symptom (Table 2).

Table 2: Classification of patients according to glycemic status in relation to stroke.

Glycemic status	HbA1C	No. of cases	Ischemic stroke
Euglycemia	<4.5%	60/150	40%
Pre DM	5.7-6.4%	20/150	13%
Known DM	76.5%	70/150	46%

Table 3: Risk factor for stroke.

		Frequency	Percentage
Sex	Male	97	65(%)
	Female	53	35(%)
History of CAD	Present	45	30(%)
	Absent	105	70(%)
Diabetes	Present	60	60(%)
	Absent	90	40(%)
HTN	Present	120	80(%)
	Absent	30	20(%)
Dyslipidemia	Present	98	65(%)
	Absent	52	34(%)
Smoking	Present	67	44(%)
	Absent	83	55(%)
Microalbuminuria		46	

Out of 150 patients, 66 cases (44%) of stroke occur in age group of 51-60 years, another 36 cases 24% occurred in

age group 61-70 years. This show commonest age group is 51-60 years (Table 3). For ischemic stroke observed in our study. We had 120 patients of HTN,

microalbuminuria is present in 44 patients (36%), the HTN patients had 8 times higher risk of MA (ODD Ratio 8.2; 0.95% C.L.; (1.8-31.9), p value 0.018 (significant).

Table 4: Relationship of hypertension / diabetes / dyslipidemia / smoking with microalbuminuria.

		Microalbuminuria		Odd ratio (95% CL)	p value
		Normal albuminuria	Micro-albuminuria		
HTN	No	28	02	8.2	0.018
	Yes	76	44	(1.8-31.9)	
DM	No	85	05	30	<0.001
	Yes	20	40	(9.6-78.8)	
Smoking	No	77	06	7.1	0.016
	Yes	43	24	(1.2-22.8)	
Dyslipidemia	No	42	10	1.07	0.175
	Yes	78	20	(0.8-4.0)	

(p < 0.005 significant).

In this study, diabetes mellitus was on important risk factor for microalbuminuria, (Table 4) microalbuminuria is observed in 40 (33%) patients of DM as compared to 120 patients of euglycemic (ODD ratio 30:95% C.L. (9.6-78.8), p value 0.001 (significant). Smoking is also a contributing factor for microalbuminuria. We observed microalbuminuria in 24 (35%) patients out of 67 smoker patients with (ODD Ratio 7.0:95% C.L. (1.2-22.8), p value 0.016 (significant).

The patient who had dyslipidemia, had lower incidence (non-significant) contribution for microalbuminuria. We have observed 90 patients of dyslipidemia, 20 patients had microalbuminuria, (ODD Ratio 1.07: 95% C.L. (0.8-4.0) p value <0.175 (non-significant).

Table 5: Relationship of creatinine clearance and microalbuminuria.

GFR (mL /mint/1.73m ²)	<30 mg/gm	30-300 mg/gm	>300 mg/gm
>90	104 (patient)	Nil	Nil
60-89	Nil	Nil	Nil
45-59	Nil	38 (patients)	06 (patients)
30-44	Nil	Nil	02
15-29	Nil	Nil	Nil
<15	Nil	Nil	Nil

CrCL Cock-Croft-Gault Equation

$$\text{CrCL (mL/mint)} = \frac{140 - \text{age} \times \text{body weight}}{72 \times \text{Pcr (mg/dL)}}$$

Microalbuminuria was present in 38 patients who had high normal serum creatinine (1.2-1.4 mg/dL) with creatinine clearance of 45-59 mL/mint/1.73m², only 2 patients out of 150 patients had macroalbuminurea with serum creatinine (1.4-1.6 mg%) cr.cl-30-44 mL/mint/1.73m² (Table 5).

DISCUSSION

According to our study, risk factor for ischemic stroke are HTN, DM and smoking had microalbuminurea 36%, 60%, 35% respectively. The patients who had DM have 30 times more risk of microalbuminuria than general population. The 38 patients who had creatinine clearance (CrCl) between 45-59 /mL/mint/1.73m² had microalbuminuria of more than 30 mg/dL. It is an independent relationship between creatinine clearance and microalbumin in newly diagnosed hypertensive and type II diabetes mellitus.¹¹

In present study creatinine clearance has shown slight positive correlation with microalbuminuria. The serum creatinine was in high normal range with creatinine clearance of 45-59 /mL/mint/1.73m². Hence, even minor decrement in GFR result, presence of microalbuminuria, is now recognized risk factor for cardiovascular disease.¹²

Smoking was independently associated with microalbuminuria and its prevalence is almost double in smoker than non-smoker with primary HTN.^{13,14} The HOPE study, document smoking is an independent determinant of microalbuminuria in DM and non-DM patients with high cardiovascular profile.¹⁵

Although previous studies had shown proteinuria as an independent predictor of stroke outcome in general population, none have examined the possible association between microalbuminuria and incident of stroke.^{16,17}

Microalbuminuria is independently associated with carotid artery intima-media thickness in non-DM individual in insulin resistance and atherosclerosis study, USA.¹⁸ The Epic Norfolk study is the 1st report evaluating the prospective relationship between microalbumin and fatal and non-fatal cerebrovascular accidents in general population.¹⁹

Still observation studies cannot prove causality and mechanistically it is unclear how albuminuria would directly cause stroke. It is more likely that albuminuria and stroke closely share similar underlying pathophysiological process (e.g. generalized endothelial dysfunction and enhance the penetration of lipoprotein into arterial wall, and albuminuria and cerebrovascular diseases are not casually related but rather reflect common determinants.²⁰⁻²²

CONCLUSION

Microalbuminuria can serve as useful risk marker for generalized vascular endothelial dysfunction and early renal impairment. Test for urine microalbumin is simple and relatively cheap, for assessing underlying vascular endothelial dysfunction and extrapolating vascular event.

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Ethical approval: The study was approved by the institutional ethics committee

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