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MICROALBUMINURIA;

AMONG PATIENTS WITH ACUTE ISCHEMIC STROKE ADMITTED IN TERTIARY CARE HOSPITAL.

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ABSTRACT... Objectives: To determine the frequency of microalbuminuria in patients with acute ischemic stroke. **Study Design:** Cross-sectional study. **Setting:** Medical floor, Independent University Hospital, Marzipura, Faisalabad. **Study Duration:** Two years, from 1st October 2013 to 30th September 2015. **Materials and Methods:** 95 patients of ischemic stroke, with or without diabetes mellitus and hypertension were tested for early morning urine albumin to creatinine ratio, after excluding patients with raised serum creatinine, urinary tract infection, congestive heart failure and menstruation. A urinary albumin to creatinine ratio of 30 to300 μg/mg was considered as MA. **Results:** Out of a total of 95 patients, MA was present in 46(48.4%) and absent in 49(51.6%) patients. Out of 33 diabetic patients, MA was present in 18(54.5%) patients while out of 62 non-diabetics 28(45.2%) had MA. Out of 55 hypertensive patients, MA was present in 27(49.1%) while out of 40 non-hypertensives 18(45.0%) had MA. Among 14 patients having both diabetes mellitus and hypertension, 8(57.1%) were having MA. Out of 20 patients without both diabetes and hypertension, 8(40.0%) had MA. **Conclusion:** Given the high frequency of microalbuminuria in patients with ischemic stroke, microalbuminuria is a useful modifiable factor in addition to conventional risk factors in identifying those at increased risk of ischemic stroke.

Key words: Albuminuria, Diabetes Mellitus, Hypertension, Ischemia, Stroke.

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INTRODUCTION

Ischemic stroke, third most common and the leading cause of physical disability worldwide. About 2/3rd in low and middle-income countries. Mortality following stroke is 20–25%.It is defined as a syndrome with sudden onset of cerebral deficit due to vascular cause lasting more than twenty four hours.[1] Prevalence of stroke in Pakistan population reported to be 4.8%.[2] Modifiable risk factors for stroke are hypertension, diabetes mellitus, smoking and increased cholesterol level.[3] Other risk factors include alcohol consumption in heavy amount, illicit drug use and age more than 55 years.[4]

In ischemic stroke, mainly atherosclerosis of the arteries supplying central nervous system is believed to be theetiological factor. Microalbuminuria (MA) defined as albumin concentration of 30 to 300 mg/day in a 24-hour urine collection or 30 to 300 μg/mg creatinine in a spot urine sample (preferred method), is considered to be associated with atherosclerosis.[5,6,7] The proposed mechanism of microalbuminuria leading to clinical vascular disease is increased systemic vascular permeability due to endothelial damage caused by systemic atheroma formation. Microalbuminuria is believed to be a major independent risk factor for cardiovascular disease as well as for ischemic stroke.[8] In various international studies, 46-50% of patients with ischemic stroke have microalbuminuria.[9,10] Moreover in normal healthy persons microalbuminuria is found frequently (5 - 7%).[11]

Therefore, microalbuminuria may be a useful marker in preventing ischemic stroke in primary health care. This study has been planned to observe the frequency of MA in local population with acute ischemic stroke. Independent Medical College/ Independent University Hospital has a

very large referral area in local vicinity i.e, Marzipura from Faisalabad main city, and adjoining areas of Chiniot, Narwala Bangla and different chaks from Narwala Bypass. Thereby with this screening and early institution of therapy for MA we can prevent ischemic stroke and decrease morbidity and mortality from such a dreadful event.

METHODOLOGY

This cross-sectional study was conducted at the medical floor of Independent University Hospital Faisalabad, a tertiary care teaching hospitalattached to Independent Medical College, Faisalabad having 550 beds with all necessary facilities. The study was completed over a period of 24 months from 1st October 2013 to 30th September 2015. A total of 95 non-randomized patients presented in emergency / outdoor with focal neurological deficit and evidence of infarction on CT scan brain within 72 hrs of admission were taken as cases of acute ischemic stroke. Obtaining an informed written consent from patient or a first degree relative where patient was not able to give own consent. An albumin to creatinine ratio (ACR) of 30 to300 µg/mg in a spot urine sample was considered as microalbuminuria. All ischemic stroke patients with or without diabetes mellitus, with or without hypertension, whether smoker or non-smoker and with or without hypercholesteremia were included. All patients with plasma creatinine > 1.2mg/dl, urinary tract infection, congestive cardiac failure and all menstruating women were excluded. Data was analyzed using SPSS version. Patients were divided according to age into four age groups. Age group 1 had patients aged 26-40 years, group 2 had patients aged 41-55 years, group 3 had patients aged 56-70 years, and group 4 had patients aged 71-85 years.

RESULTS

A total of 95 patients with acute ischemic stroke were included in the study. There were 51(53.7%) male and 44(46.3%) female patients. Minimum age was 26 years and maximum age was 84 years. These patients were distributed in 4 different age groups. Group 1 (26-40 years) had 10 patients (10.5 %), group 2 (41-55 years) had 39 patients (41.1 %), group 3 (56-70 years) had 41 patients (43.2 %) and group 4 (71-85 years) had 5 patients (5.2%) (Table-I). Among a total of 95 patients, minimum duration of ischemic stroke was 2 hours while maximum duration was 72 hours with a mean duration of 13.80 hours and SD of 9.9 hours. Minimum ACR was 2.76µg/mg while maximum ACR was 298.50 µg/mg with a mean ACR of 63.54 µg/mg and SD of 66.63 µg/mg. Among a total of 95 patients, 33(34.7%) were diabetic while 62(65.3%) were non-diabetic. 55(57.9%) patients were hypertensive while 40(42.1%) were non-hypertensive.

Age	Frequency	Percent
26-40	10	10.5
41-55	39	41.1
56-70	41	43.2
71-85	5	5.2
Total	**95**	**100.0**

Table-I. Distribution of patients according to their age

Among a total of 95 patients, MA was present in 46(48.4%) patients while MA was absent in 49(51.6%) patients. Among a total of 46 patients with MA, age group 1 (26-40 years) had 4 patients (8.7 %), group 2 (41-55 years) had 18 patients (39.2 %), group 3 (56-70 years) had 22 patients (47.8 %) and group 4 (71-85 years) had only 2 patients (4.3%) (Table-II). These observations revealed that relatively older patients (age> 55 years) had maximum number of patients with MA.

Microalbuminuria	Age	Frequency	Percentage
Present	26-40	4	8.7
	41-55	18	39.2
	56-70	22	47.8
	71-85	2	4.3
	Total	46	100.0
Absent	26-40	6	12.2
	41-55	21	42.8
	56-70	19	38.8
	71-85	3	6.2
	Total	49	100.0

Table-II. Distribution of Microalbuminuria in different age groups

Among 51 male patients, MA was present in 23(45.1%) patients while it was absent in

28(54.9%) patients. Among 44 female patients, MA was present in 23(52.3%) patients while it was absent in 21(47.7%) patients (Table-III). This shows that MA was slightly more common in females than males.

Gender	MA	Frequency	Percent
Male	present	23	45.1
	absent	28	54.9
	Total	51	100.0
Female	present	23	52.3
	absent	21	47.7
	Total	44	100.0

Table-III. Distribution of Microalbuminuria according to gender

Among a total of 33 diabetic patients, MA was present in 18(54.5%) patients while it was absent in 15(45.5%) patients. Out of 62 non-diabetics 28(45.2%) had MA while 34(54.8%) had not (Table-IV). This shows that MA was more common in diabetics than non-diabetics.

Diabetes Mellitus	MA	Frequency	Percent
Present	present	18	54.5
	absent	15	45.5
	Total	33	100.0
Absent	present	28	45.2
	absent	34	54.8
	Total	62	100.0

Table-IV. Distribution of Microalbuminuria according to Diabetes Mellitus

Among a total of 55 hypertensive patients, MA was present in 27(49.1%) patients while it was absent in 28(50.9%) patients. Out of 40 non-hypertensives 18(45.0%) had MA while 22(55.0%) had no MA (Table-V). This shows that MA was slightly more common in hypertensive as compared to non-hypertensive patients.

Hypertension	MA	Frequency	Percent
Present	present	27	49.1
	absent	28	50.9
	Total	55	100.0
Absent	present	18	45.0
	absent	22	55.0
	Total	40	100.0

Table-V. Distribution of Microalbuminuria according to Hypertension

Among a total of 19 patients having diabetes without hypertension MA was present in 10(52.6%) while it was absent in 9(47.4%) patients. Similarly out of 41 patients having hypertension without diabetes, 19(46.3%) patients were having MA while it was absent in 22(53.7%) patients. This shows that diabetes alone is linked with greater prevalence of MA than hypertension alone.

Among a total of 14 patients having both diabetes and hypertension, 8(57.1%) patients were having MA while it was absent in 6(42.9%). This showed that chances of having MA were increased in the presence of both diabetes and hypertension. Among a total of 20 patients without both diabetes and hypertension, 8(40.0%) patients were having MA while it was absent in 12(60.0%) patients. This showed that even if patients were not having diabetes and hypertension, a significant number of patients had MA.

These patients were also divided in 3 different income groups. Group 1(<15,000 Rs. /month) had 40 patients (42.1%), group 2(15,000-30,000 Rs. /month) had 46 patients (48.4%) and group 3 (>30,000 Rs. /month) had 9 patients (9.5%). Among a total of 46 patients with MA, group 1(<15,000 Rs./month) had 19 patients (41.3%), group 2(15,000-30,000 Rs./month) had 24 patients (52.2%) and group 3 (>30,000 Rs./month) had 3 patients(6.5%)(Table-VI). These observations reveal that people of higher socioeconomic class had less number of patients with MA as compared to low and middle socioeconomic status.

MA was more frequent in first 24 hours when plotted according to duration of ischemic stroke.

Income in Rs/month	MA	Frequency	Percent
<15000	present	19	47.5
	absent	21	52.5
	Total	40	100.0
15000-30000	present	24	52.2
	absent	22	47.8
	Total	46	100.0
>30000	present	3	33.3
	absent	6	66.7
	Total	9	100.0

Table-VI. Distribution of microalbuminuria according to socioeconomic status

DISCUSSION

During the past years epidemiologic and experimental studies show that microalbuminuria is associated with increased riskfor all-cause and cardiovascular mortality, cerebrovascular disease, and possibly, peripheral arterialdisease. Ourstudy results revealed that MA was present in 48.4% of patients with ischemic stroke. Among non-diabetics 45.2% of patients had MA. These results are in accordance with international studies like conducted by Slowik et al in which MA was found in 46.7% and Turaj et al in which incidence of MA was 46.1% as well as local study in which MA was present in 47.1 % non-diabetic, hypertensive patients with acute ischemic stroke.[12,13,14] In another study by Beamer et al in United States, MA was found in 29% of acute stroke patients within 7 days of onset of symptoms and in 10% of controls indicating that MA was 3 times more prevalent in patients with recent stroke than in those with clinical risk factors for stroke.[15] In an Indian study by Mathur et al, MA was found in 68% of acute non-diabetic ischemic stroke patients.[16] This study limitations included small sample size, however authors attributed the higher incidence of MA, as compared to western studies, to higher fibrinogen, Von Willebrand and t-PA levels in South Asian ischemic stroke patients along with racial differences, higher incidence of smoking, altered lipid profile and strenuous physical activity in South Asians.

In British population, study conducted by Yuyun and his colleagues, in multivariate analysis found that MA was only independent predictor of ischemic stroke (HR 2.01;95% CI 1.29 to 3.31) and concluded that it was independently associated with approximately 50% increased risk of stroke in general population.[9] My study results support these findings.

In this study frequency of MA increased to 54.5% in diabetic patients and 49.1% in hypertensive patients alone. In the presence of both diabetes and hypertension frequency of MA arose to 57.1%. These results are in accordance with the study by Beamer et al.[15] Prevalence of MA in hypertensive patients with ischemic stroke was also found to be significantly higher in my study than in hypertensive patients alone without ischemic stroke where microalbuminuria can be detected in about 30% of patients with mild or moderate hypertension, ranging from 7% to 40% depending on age and ethnic group.[17]

My study results showed that even after adjusting for Diabetes and hypertension 40.5% patients were having MA. This shows that MA is quite frequent in ischemic stroke patients even when major risk factors such as diabetes and hypertension are excluded. This conclusion is in accordance with other studies like EPIC-Norfolk study and study of Beamer et al.[9,15] Such a high prevalence of MA can be partly due to presence of other risk factors like smoking and hypercholesterolemia which are linked with both stroke and MA.[18]

In our study frequency of MA increased with advancing age upto 70 years and afterthat declined. This can possibly be attributed to decreased survival of patients in older age group so that only 5 patients were above 70 years of age in my study. A positive correlation of advancing age and MA in patients with acute ischemic was found in other studies also.[9,15,16] Similarly, positive correlation of advancing age and MA in patients with risk factors for cardiovascular disease was found in the studies of Chowta NK and his colleagues, Metcalf P and his colleagues, the Takahata study and a systemic literature review by Dinneen and Gerstein.[19-22]

The results of my study showed that MA was less common in patients of higher socioeconomic class (9.5%) as compared to low and middle class (42.1% and 48.4%). This difference may be explained on basis of better compliance to treatment of diabetes and hypertension in patients with higher socioeconomic class as they are deemed to be linked to MA in ischemic stroke patients.Moreover, number of patients with higher socioeconomic class is low because of the area which our hospital mostly covering is related to poor and low socioeconomic population. My study results revealed that MA was more common in first 24 hours after ischemic stroke. Similar

findings were noted by Mathur et al.[16] This may be partially as a consequence of inflammatory reaction that involves renal system in patients with ischemic stroke.

The mechanism of the association between MA and cerebrovascular disease is still largely unknown and a focus of research and debate. Several explanations have been suggested; MA may reflect generalized endothelial dysfunction that might enhance penetration of atherogenic lipoproteins into the arterial wall.[23,24] As my study results revealed that the frequency of MA in patients with ischemic stroke is significant, MA screening in general population with additional risk factors for cerebrovascular disease should be a routine so that with early pharmacological intervention we may be able to decrease the morbidity and mortality in this group of patients.

CONCLUSION

There was a high frequency of microalbuminuria in patients with ischemic stroke. This is a useful modifiable factor in identifying those at increased risk of ischemic stroke. Although there is evidence of an increase in mortality risk with MA that is independent of diabetes and hypertension, screening for MA in the general population of nondiabetic patients without any risk factors is not yet recommended, since the value of screening in these patients is unclear and the ability of any therapies to provide benefit in this setting is unknown. Further interventional, prospective studies are required to answer this issue.

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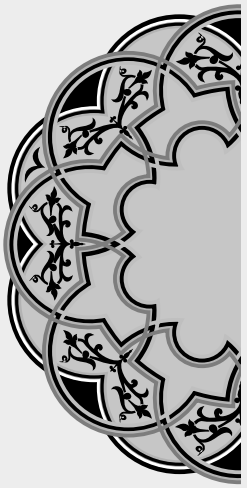

"Respect is for those who deserve it,
Not for those who demand it."

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Muhammad Zakria	Data collection, Results, Discussion, References	
2	Dr. Muhammad Sarfraz	Lab Investigation	
3	Dr. Touseef Ahmad	Results	