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Level of Albumin Creatinine Ratio (ACR) Among the Hospitalized Stroke Patient

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Abstract: *Stroke is the third leading cause of death and the most prevalent disabling neurologic disease. Urinary albumin creatinine (UACR) ratio in spot urine sample can be assessed as an early predictive factor for stroke risk determination. A cross sectional study was performed on 117 patients with stroke as case at Chittagong Medical College Hospital, Bangladesh and 117 individuals of their relatives and/or accompanying family members without history of cardiovascular disease as healthy control. Spot urine samples were obtained from both groups and urinary creatinine and albumin were measured. Mean values for urinary albumin-creatinine ratio were higher in the case group compared to healthy controls. There was a significant correlation between urinary albumin creatinine ratio and stroke event (P = 0.001). UACR were also found higher among the patients who had different risk factors of stroke like DM, hypertension, and ischemic heart disease. There is positive correlation between urine albumin creatinine ratio (ACR) and stroke.*

Keywords: *Albumin creatinine ratio, Stroke, Microalbuminuria.*

I. Introduction

The world health organization defines stroke as "the rapidly developing clinical symptoms and or signs of focal (at times global) disturbance of cerebral function, with symptoms lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin[1]. One in every 10 deaths is caused by stroke; thus it is the third most common cause of death in developed countries, exceeded only by coronary heart disease and cancer [2]. The prevalence of stroke in the US is about 7 million (3.0%) [3]. Worldwide, China has one of the highest rates of mortality (19.9% of all deaths in China), along with Africa and parts of South America [4]. The World Health Organization ranks Bangladesh's mortality rate due to stroke as number 84 in the world [5]. A recently published data suggests the prevalence of stroke in Bangladesh is 5 to 12 per 1000 population (about 1% of population). The high number of disability-adjusted life-years lost due to stroke (485 per 10,000 people) show that stroke severely impacts Bangladesh's economy [5]. In Bangladesh the estimated economic loss stands to 408 million US dollar per year due to stroke morbidity and mortality [6]. Risk factors for stroke include advanced age, microalbuminuria, hypertension, previous stroke or transient ischaemic attack (TIA), diabetes mellitus, high cholesterol, cigarette smoking, atrial fibrillation, migraine with aura, and thrombophilia [7].

Microalbuminuria, a marker of both kidney disease and endothelial dysfunction, may be associated with global vascular risk. The pathophysiologic processes that link microalbuminuria and cerebrovascular disease (CVD) are unclear. Microalbuminuria could be a cause or a consequence of vascular disease. In the STENO hypothesis [8], albumin leakage into the urine is a reflection of widespread vascular damage. In a sense, the kidney is the window of the vasculature. In view of these considerations, endothelial function and chronic inflammation have been suggested as possible candidate to explain the association between microalbuminuria and CVD. Other studies indicate that although microalbuminuria, endothelial dysfunction, and low-grade inflammation are linked, they all are independently associated with risk for cardiovascular death.[9] More recently, a highly significant association between microalbuminuria and carotid artery intima-media thickness has been reported, a finding which suggests that microalbuminuria may be a marker for early development of carotid artery atherosclerosis and points to a possible linkage between microalbuminuria and atherothrombotic stroke mechanism [10].

The **albumin/creatinine ratio (ACR)** is done to compare the amount of albumin passing into the urine compared to the amount of creatinine present. Whenever the value of ACR is more than 30 mg but less than 300 mg of albumin per gram of creatinine will be termed as microalbuminuria. An albumin level above the upper limit value is called "macroalbuminuria", or sometimes just albuminuria [11]. The advantage of this test is that this ratio remains unaffected by any kind of variation in the concentration in urine. Four different sampling methods are used to diagnose microalbuminuria that is 24-h urine collection, overnight-timed urine collection, spot morning urine collection, and finally random spot sampling [12].

As creatinine is produced by the muscle, so in a person with too much or too little muscle mass the test may produce inaccurate result. The test may also herald false impression in case of pregnancy, menstruation or vaginal discharge, high protein intake, heavy exercise within 24 hours, drugs (like NSAIDs. ACE inhibitors especially captopril etc), diseases that related with macroproteinuria and some others co-morbid diseases like febrile illness, CCF, UTI, AKI, CKD, etc [13].

Despite the advent of newer treatment and intervention effective prevention remains the best treatment for reducing the burden of stroke. It has been claimed that atherosclerosis may be the most common (approximately 50%) cause of stroke worldwide [14]. As a result to reduce the burden of stroke management strategies are increasingly focusing on preventive measures following early detection of markers of atherosclerosis. Microalbuminuria, is gaining recognition as a simple marker of an atherogenic milieu. If the patients or physicians could predict the microalbuminuria earlier, the progression and adverse consequence of atherosclerosis could be minimized. In our setting there are scarcities of studies regarding the estimation of ACR in stroke patients. So this study is aimed at to find out ACR in a group of hospitalized stroke patients.

II. Material And Methods

A cross sectional comparative study was done from July 2012 to June 2013 at Medicine and Neurology department of Chittagong Medical College Hospital, Chittagong Bangladesh. Inclusion criteria are CT/MRI proved stroke patient, age more than 18 years and within 48 hours of stroke attack. Exclusion criteria are recurrent stroke, pregnant women, co morbid diseases that causes Microalbuminuria (UTI, CCF, AKI, CKD), menstruating women. After fulfillment of selection criteria 117 (one hundred and seventeen) stroke patients were taken along with 117 (one hundred and seventeen) healthy controls. His/her legal attendant were thoroughly informed about the aims, objectives and detail procedure of the study before examination. She/he was encouraged for voluntary participation.

Healthy matched controls were selected from the attendant, relatives or those who voluntarily agreed to be included in the study. They were recruited on the basis of history and absence of documented medical diseases. After getting consent clinical history were taken and clinical examination were done to elicit findings related to stroke and its complications. Related investigations like urine examination with colony count, blood glucose, and serum creatinine were done. Spot urine sample for ACR was taken. Five (5) ml of urine was collected. Sample was sent to the laboratory within 30 minutes of collection. The patients/ attendants/ volunteers were asked to avoid exertion prior to urine collection. In women, urine was collected during the non menstrual phase of their cycles. In case of catheterized patient urine was collected from distal end of catheter from continuous flow and not from pooled urine. ACR was carried out by using immunonephelometric method in Vitros 350 (J & J) Olympus AU 640 Chemistry Analyzer.

III. Data collection and analysis

All relevant information for each individual study subject was recorded after getting informed written consent on a pre- tested data sheet. Collected data were checked repeatedly. The continuous data were assessed by mean, range and standard deviation (SD). The discrete data were assessed in number and percent. Discrete or qualitative variables were analyzed by Chi-squared test and continuous variables were analyzed by t- test. P-value < 0.05 represented statistical significance. Statistical analysis was assessed by using computer based statistic program, SPSS (Statistical Package for Social Science) version 19.0.

IV. Results

1. Gender distribution of the patients: Gender were matched with study subjects and control group (p>0.05)

Table I: Distribution of Respondents according to Sex (N=234)

	Sex		
Type of subject	**Male**	**Female**	**Total**
Case	64 (54.7%)	53 (45.3%)	**117 (100%)**
Control	59 (50.4%)	58 (49.6%)	**117 (100%)**
Total	**123 (52.6%)**	**111 (47.4%)**	**234 (100%)**

*p=0.513(Chi square test)

2. Analysis of the risk factors of the study patients: Regarding risk factor analysis of stroke, hypertension (61.54%), DM (34.2%), cigarette smoking (30.8%) and dyslipidemia (17.9%) were found common.

Table II: Risk factors of stroke, (N=117)

Risk factors	Frequency		Total
	Male	Female	
Hypertension	43 (36.75%)	29 (24.79%)	72 (61.54%)
DM	24 (60%)	16 (40%)	40 (34.2%)
Cigarette smoking	28 (77.77%)	08 (22.23)	36 (30.8%)
Family history of stroke	18 (54.54%)	15 (45.46%)	33 (28.2%)
Dyslipidemia	13 (61.9%)	08 (38.1%)	21(17.9%)
Peripheral vascular disease	02 (100%)	00	02 (1.7%)
Pre-existing heart disease	9 (50%)	9 (50%)	18 (15.38%)

3. Pattern of ACR among the Respondents: ACR was found significantly high ($p<0.05$) among the study population than control group but insignificant association was found among the stroke type and gender.

Table IIIa: Pattern of ACR in term of Albuminuria (N=234)

Pattern of ACR	Type of Respondents		Total
	Case (N=117)	Control (N=117)	
No microalbuminuria (<30 mg/gm)	67 (57.3%)	97 (82.9%)	164 (70.1%)
Microalbuminuria (30-300 mg/gm)	48 (40.2%)	20 (17.1%)	68 (28.6%)
Macroalbuminuria (>300 mg/gm)	2 (02.6%)	0 (0.0%)	2 (01.3%)

P=0.001(Chi square test)

Table IIIb: Pattern of ACR (mg/gm) in term of value (N=117)

	Type of Respondents	Mean	Std. Deviation	P value*
ACR (mg/gm)	Study subjects	63.25	± 38.32	0.001
	Control	29.74	± 24.22	

*P value was calculated by independent sample t- test

Table IIIc: Pattern of ACR (mg/gm) among different types of stroke (N=117)

Clinical diagnosis	N	Mean	Std. Deviation	P value*
Ischaemic	78	63.78	± 43.14	0.916
Hemorrhagic	39	62.16	± 30.80	

*P value was calculated by independent sample t- test

Table IIId: Pattern of ACR (mg/gm) among the genders (N=234)

ACR (mg/gm)				
Sex	Mean	N	Std. Deviation	P value*
Male	44.3993	123	± 30.45	0.657
Female	49.7211	111	± 38.25	
Total	46.9238	234	± 34.32	

*P value was calculated by independent sample t- test

Table 4: **Frequency of microalbuminuria in relation with age change among the respondents:** Microalbuminuria was found more common among 50-60 years (28.6%) and 60-70 years (29.9%) age group.

Table IV: Frequency of microalbuminuria in relation with age change among the respondents. (N=234, case-117, control117)

Age group (Years)	Microalbuminuria		
	No microalbuminuria	Microalbuminuria	Total
20-29	2 (1.2%)	0 (0.0%)	2 (0.9%)
30-39	6 (3.6%)	1(1.4%)	7 (3.0%)
40-49	19 (11.5%)	7(10.1%)	26 (11.1%)
50-59	45 (27.3%)	22 (31.9%)	67 (28.6%)
60-69	52 (31.5%)	18 (26.1%)	70 (29.9%)
70-79	28 (17%)	6 (8.7%)	34 (14.5%)
>80	13 (7.9%)	15 (21.7%)	28 (12%)
Total	165 (100.0%)	69 (100.0%)	234 (100.0%)

5. Association of ACR with different risk factors: Association of ACR with different risk factors of stroke was found significant (P<0.05) in hypertension (OR-2.762), DM (OR-1.829), pre-existing heart disease (OR-3.695) & family history (OR-1.642) but insignificant (P>0.05) in smoking (OR-0.939), peripheral vascular diseases (OR-0.347) and lipid profile (N=117)

Table V: Association of ACR with risk factors of stroke analyzed by Logistic Regression Analysis (N=117)

Risk factors		Microalbuminuria		OR	CI	P value
		Absent	Present			
Hypertension	Yes	33 (45.8%)	39 (54.2%)	2.762	1.250-6.105	0.04
	No	30 (65.2%)	16 (34.8%)			
Diabetes	Yes	14 (35.0%)	26 (65.0%)	1.829	0.844-3.963	0.005
	No	48 (62.3%)	29 (37.7%)			
Cigarette smoking	Yes	18 (50.0%)	18 (50.0%)	0.939	0.424-2.079	0.67
	No	44 (54.3%)	37 (45.7%)			
Family history	Yes	12 (36.4%)	21 (63.6%)	1.642	0.730-3.695	0.024
	No	50 (59.5%)	34 (40.5%)			
Peripheral Vascular disease	Yes	01 (50.0%)	01 (50.0%)	0.347	0.082-22.069	0.674
	No	66 (58.3%)	49 (41.7%)			

Figure: 1 Relation of ACR with change of Systolic Blood Pressure (SBP): Regarding Relation of ACR with Systolic Blood Pressure (SBP) showing change of SBP causes positive increase of ACR

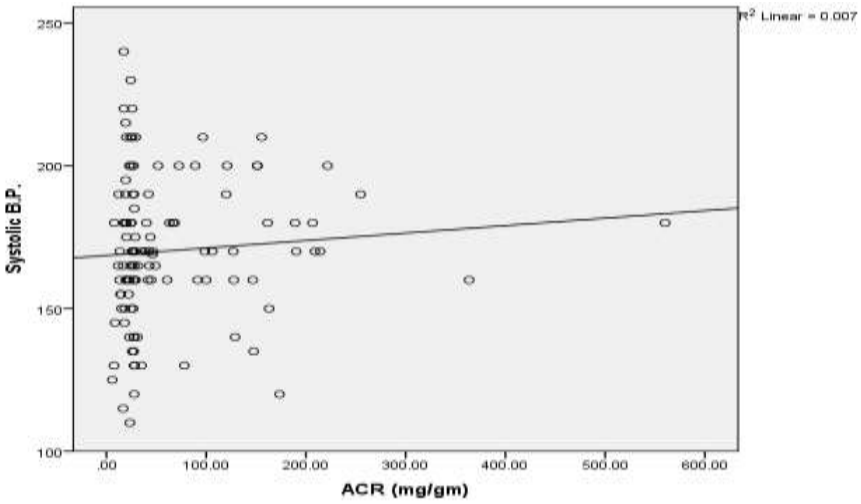
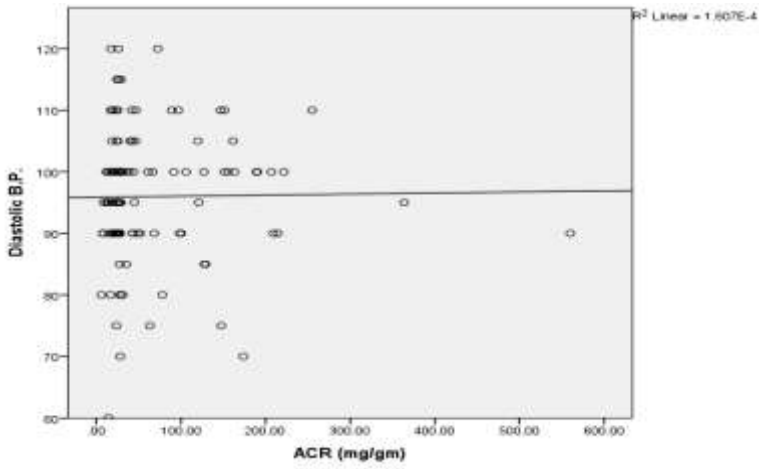


Figure: 2 Relation of ACR with change of Diastolic Blood Pressure (DBP): Regarding Relation of ACR with DBP showing change of DBP causes positive increase of ACR



V. Discussion

This cross sectional study was done among the admitted stroke patients to evaluate the level of Albumin Creatinine Ratio (ACR). In the study, 117 stroke patients were enrolled and same numbers of healthy people were also taken as control. The mean age of the case and control was 62.41 and 59.70 years respectively. The prevalence of stroke is higher among men in comparison with women (Male female ratio is 1.20:1). A study carried out at Mymensingh Medical College Hospital by Mohammed et al [15], stroke prevalence was also found to be higher among in men (Male female ratio, 1.43:1). Epidemiological studies have shown that stroke is more common in men than in women. A study done by Peter Appelros [16], et al, among stroke patients of 19 countries in 5 continents shows that the pooled age adjusted rate of Male/female stroke ratio was 1.33, meaning that stroke is 33% more incident in males than females. Regarding risk factor analysis of stroke patients, hypertension, DM, cigarette smoking, family history and dyslipidemia were found common [Table-II]. A study [17] done in Allied Hospital, Faisalabad where diabetes mellitus and hypertension, were found as common risk factors of stroke which is consistent with present study as expected.

More microalbuminuria cases were found among those who had higher duration of smoking (31.14 years), DM (11.80 years) and Hypertension (8.68 years). [Table-III]. Also more duration with different risk factors influenced to development of microalbuminuria. Long term insult to the vessel produces more changes in the glomerular bed which might influence the leakage of protein. A study [18] done by Rodicio et al concluded that hypertension, DM, cigarette has positive influence on the development of microalbuminuria which subsequently progress to vascular diseases like cerebral, renal or cardiac disease. A study done by Gupta [19] et al, microalbuminuria and urinary ACR level were directly related to the amount of smoking pack years, on the other hand an observational study [20] shows that the predictive value of microalbuminuria was highly dependent on duration of diabetes, with the risk for development of macroalbuminuria being up to 10% per year in patients with 10 to 15 years' duration of diabetes. Prevalence of an elevated UAE increases with age, and with longer duration and a higher severity of hypertension. A Study [18] on essential hypertension shows that microalbuminuria can be found in up to 40% of untreated hypertensive population. ACR was found significantly high ($p<0.05$) among the study population (case) than the control group (Table IIIa) and mean value of ACR (63.25 ± 38.32 mg/gm) also in higher level in comparison with the control group ($p < 0.001$) [Table-IIIb]. So it can be said that urinary albumin loss is more prominent in stroke patients than the control group. A study among the stroke patients done in Iran [21] found that albumin-creatinine ratio was higher in the case group compared to healthy controls. There was a significant association between average albumin creatinine urinary excretion ratio and stroke ($P = 0.02$). So this study findings regarding association of stroke with level of ACR is consistent with present study. The prevalence of microalbuminuria reported by Slowik et al. in patients within 24h after acute stroke was 46.7% [22]. This is similar with Turaj et al. who reported prevalence rate of 46.1% within 24h after acute stroke ($p=0.05$) [23]. Regarding analysis of clinical diagnosis of stroke microalbuminuria is more common in ischemic stroke than hemorrhagic [Table-IIIC]. This findings are consistent with a study [17] carried out by Farooq et al at Allied Hospital Faisalabad among 195 ischemic stroke patients, found microalbuminuria in 94 (44.2%) patients. Changes of age were found to be associated with more frequent microalbuminuria [Table - IV]. A study done by Johsen[23] found a significant difference in relative frequency of microalbuminuria in relation with age changes. Microalbuminuria in different risk factors of stroke like hypertension, DM, cigarette smoking, family history and peripheral vascular disease were found 54.2%, 65%, 50%, 63.6% and 50% respectively. Among them hypertension (OR-2.762, CI=1.250-6.105), DM (OR-1.829, CI=0.844-3.963) & family history (OR-1.347, CI=0.730-3.695) were found more significant but insignificant in smoking (OR=0.939, CI=0.424-2.079), peripheral vascular diseases (OR=0.347, CI=0.082-22.069) [Table-V]. A study done by Mattock et al [24] shows that microalbuminuria in essential hypertension is 53% to 71% and highest in uncontrolled diseases. This finding has adequately confirmed our result (54.2%).

Regarding Relation of ACR with Blood Pressure showed that change of both Systolic and diastolic blood pressure causes positive increase of ACR [Figure-I & Figure-II] where systolic blood pressure change is more significant (r^2 linear 0.007). A Study done by Cirillo et al, [25] shows that Pulse pressure and isolated systolic hypertension were significantly related to urinary albumin excretion and the prevalence of microalbuminuria in univariate and multivariate analyses. This finding also Support our result.

VI. Conclusion

Stroke is a common cerebrovascular disease which causes significant mortality and morbidity. It is the leading cause of adult disability and the third leading cause of mortality worldwide. There are several risk factors for stroke such as diabetes, hypertension, smoking, hyperlipidaemia, old age, lack of exercise etc. Each of these risk factors leads to atherosclerosis which is the main underlying mechanism of development of stroke. To reduce the burden of stroke, management strategies are now focusing on preventive measures. So, early detection of atherosclerosis may be a way to prevent stroke. On this ground microalbuminuria is an authentic marker for detection of atherogenic milieu. Estimation of Urinary Albumin Creatinine Ratio (ACR) on a spot

urine sample considered to be a simple and easy method to detect microalbuminuria. It is a noninvasive, cost effective and less time consuming test. Role of ACR in detection of atherosclerosis, the harbinger of stroke, is not yet widely thought in our country. To address this scientific issue this study is aimed at findings the association of microalbuminuria with stroke in our context. High level of ACR in term of microalbuminuria is associated with stroke risk. Ischemic or hemorrhagic stroke both are related with microalbuminuria. Risk factors of stroke like DM, HTN and pre existing heart diseases also influence the ACR. Declaration: All the authors declare no competing interest.

References

[1]. WHO MONICA Project Investigators. The World Health Organization MONICA Project (Monitoring trends and determinants in cardiovascular disease). J Clin Epidemiol 1988;41:105-114.
[2]. Mackay J and Mensah G. The Atlas of Heart Disease and Stroke. Geneva, Switzerland, World Health Organization 2004.
[3]. Roger et al. AHA Heart Disease and Stroke Statistics 2011 update: a report from the American Heart Association 2011; 123:e18-e209.
[4]. Kim AS & Johnston SC. Global variation in the relative burden of stroke and ischaemic heart disease 2011;124:314-323.
[5]. Islam MN, Moniruzzaman M, Khalil MI, et al. Burden of stroke in Bangladesh 2013;8(3):211-3.
[6]. Stroke Management Guideline. Line director, Improved Hospital Services Management & Director Hospitals & Clinics. Directorate General of Health Services, Mohakhali, Dhaka, December, 2008.
[7]. Matthew PF, Douglas CA, Umberto De G. The Central Nervous system. In: Cotran RS, Kumar V, Fausto N, Nelson F, Robbins SL, Abbas AK. Robbins and Cotran pathologic basis of disease. 7th ed. St. Louis, Mo: Elsevier Saunders Company; 2005: 678-728.
[8]. Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, et al. Albuminuria reflects widespread vascular damage. The Steno hypothesis, Diabetologia 1989;32(4):219 –226.
[9]. Jensen JS, Borch-Johnsen K, Jensen G, et al. Microalbuminuria reflects a generalized transvascular complications. Clin J Am Soc Nephrol 2007;2:581-590.
[10]. Sun-Seog Kweon, Min-Ho Shin, Young-Hoon Lee, et al. Higher normal ranges of urine albumin-to-creatinine ratio are independently associated with carotid intima-media thickness. Cardiovascular Diabetology 2012;11:112-22.
[11]. Lemley KV, Abdullah I, Myers BD. "Evolution of incipient nephropathy in type 2 diabetes mellitus". Kidney Int 2000;58(3):1228–37.
[12]. Abid O, Sun Q, Sugimoto K, et al. "Predictive value of microalbuminuria in medical ICU patients: results of a pilot study". Chest 2001;120(6):1984–8.
[13]. David W J, Graham R D, Timothy H M, et al. Consensus Working Group, Chronic kidney disease and measurement of albuminuria or proteinuria: a position statement. Med J Aust 2012;197(4):224-225.
[14]. Parving HH, Lehnert H, Bröchner-Mortensen J, et al. "The effect of irbesartanon the development of diabetic nephropathy in patients with type 2 diabetes". N. Engl. J. Med 2001;345(12):870–8.
[15]. Mohammad QD, Habib M, Hoque A, et al. Prevalence of stroke above forty years. Mymensingh Med J 2011;20(4):640-4.
[16]. Peter Appelros, Birgitta Stegmayr and Andreas Terént. Sex Differences in Stroke Epidemiology-A Systematic Review, Stroke 2009;40:1082-1090.
[17]. Muhammad Ahsan Farooq, Muhammad Sohail Anjum, Fayyaz Ahmed Malik, et al. Frequency of microalbuminuria in patients with ischemic stroke. RMJ 2013; 38(2):97-99.
[18]. Rodicio JL, Campo C and Ruilope LM. Microalbuminuria in essential hypertension. Kidney International 1998;54:851-854.
[19]. Gupta R. K, Gupta R, Maheshwari V. D, et al. Impact of smoking on microalbuminuria and urinary albumin creatinine ratio in non-diabetic normotensive smokers. Indian J Nephrol 2014;24(2):92–96.
[20]. Rossing P, Hougaard P and Parving HH. Progression of microalbuminuria in type1 diabetes: Ten-year prospective observational study. Kidney International 2005;68:1446–1450.
[21]. A Moghtaderi, E Noori and S Dabiri The association between urinary albumin and creatinine in patients with stroke. Ir J neurol 2013;12(1):121.
[22]. Slowik A, Turaj W, Iskra T, Strojny J, Szczudlik A: Microalbuminuria in nondiabetic patients with acute ischemic stroke: prevalence, clinical correlates, and prognostic significance. Cerebrovasc Dis 2002;14(1):15–21.
[23]. Turaj W, Slowik A, Wyrwicz-Petkow U, et al. The prognostic significance of microalbuminuria in nondiabetic acute stroke patients. Med Sci Monit 2001,7(5):989–994.
[24]. Mattock MB, Morrish NJ, Viberti GC, et al. Prospective study of microalbuminuria as predictor of mortality in type 2 diabetes. Diabetes 2006;41:736-741.
[25]. Cirillo M Stellato, D Laurenzi M, et al. Pulse pressure and isolated systolic hypertension Association with microalbuminuria Kidney International 2000; 58:1211–1218.

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