

## Microalbuminuria in Patients with Recent Ischaemic Cerebrovascular Stroke: A Cross Sectional Study

Shivnarayan Pattanaik<sup>1</sup> and Purna Chandra Dash<sup>1\*</sup>

<sup>1</sup>SCB Medical College, University of Utkal, Cuttack, Odisha-753001, India.

### Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

### Article Information

DOI: 10.9734/BJMMR/2016/21351

#### Editor(s):

- (1) Vijay K Sharma, Division of Neurology, Yong Loo Lin School of Medicine, National University of Singapore, National University Hospital, Singapore.
- (2) Rui Yu, Environmental Sciences & Engineering, Gillings School of Global Public Health, The University of North Carolina at Chapel Hill, USA.
- (3) Chan Shen, Department of Biostatistics, MD Anderson Cancer Center, University of Texas, USA.

#### Reviewers:

- (1) Adria Arboix, University of Barcelona, Spain.
  - (2) Pietro Scicchitano, Hospital "F. Perinei"-Altamura (Bari), Italy.
  - (3) Rajendra Nath, King George's Medical University, Lucknow, India.
- Complete Peer review History: <http://sciencedomain.org/review-history/13953>

Original Research Article

Received 13<sup>th</sup> August 2015  
Accepted 22<sup>nd</sup> March 2016  
Published 31<sup>st</sup> March 2016

### ABSTRACT

**Objectives:** Microalbuminuria is an integrated marker of both kidney disease and endothelial dysfunction may be associated with global vascular risk. The purpose of the study was to assess the association of microalbuminuria with risk of nondiabetic nonhypertensive ischaemic stroke.

**Materials and Methods:** 60 cases of recent ischaemic strokes clinically diagnosed by WHO criteria and confirmed by CT scan of brain admitted to SCB Medical College and Hospital were studied. Diabetes mellitus, family history of DM, hypertension, nephropathy, atrial fibrillation, chronic liver disease, systemic infection, neoplasm, recent myocardial infection, females during menstruation and pregnancy were excluded from the study.

**Results:** Total number of 60 patients were studied, out of which male (35)58.3% and female (25)41.6%. Most of patients were in age group between 50-70 years. Mean age of presentation with microalbuminuria was 60.71 years. Microalbuminuria present in (29)48.33% of cases as compared to (3) 10% of controls. Severity of stroke was assessed by Scandinavian Stroke scale, was lower in presence of microalbuminuria (16±9.04) than without microalbuminuria (22±12.5).

**Conclusion:** The above study shows that there is increased incidence of microalbuminuria in recent ischaemic stroke and the microalbuminuria increases with severity of stroke.

\*Corresponding author: E-mail: [purnadash@yahoo.com](mailto:purnadash@yahoo.com);

**Keywords:** Endothelial dysfunction; Microalbuminuria (MA); ischaemic stroke; scandinavian stroke scale.

## 1. INTRODUCTION

The incidence of cerebrovascular stroke is gradually increasing in all parts of world. It is the second commonest cause of death and fourth leading cause of disability worldwide. But throughout world rise in stroke risk profile, lack of awareness and lack of prevention programmes serves to widen stroke prevention gap [1]. According to WHO 2009 report in India prevalence is 90-222 per lakh population and 6,398,000 DALYs (Disability Adjusted Life Years) [2].

The realisation that atherosclerosis is an inflammatory state has lead to search for new stroke risk factors. Microalbuminuria has been associated with many diseases like diabetes, hypertension and coronary arterial disease [3,4]. With availability of relatively simple methods for detection of microalbuminuria many studies have been conducted in different parts of world as a marker of stroke risk in nondiabetic nonhypertensive population.

Microalbuminuria reflects systemic transvascular leakiness for albumin [5], which allows higher degree of lipid insudation [6] into large vessel wall linking to atherogenesis. There is a close relation between atherosclerosis, endothelial dysfunction (ED) and leakage of protein through glomerulus. In endothelial dysfunction most potent endogeneous vasodilator Nitric oxide production is hampered which leads to arterial vasoconstriction [7]. This causes increase arterial as well as glomerular pressure and permeability. In endothelial dysfunction glomerular basement membrane loses normal negative charges and loss of heparin like proteoglycan promoting thrombus formation and enhance atherosclerosis. Hence microalbuminuria is gaining recognition as a marker of atherogenic milieu and ischaemic stroke. Microalbuminuria and atherosclerosis found in endothelial dysfunction is manifested as increased intima media thickness of common carotid arteries [8,9].

Slowik et al. [10] were the first to report significant correlation between microalbuminuria and severity of stroke. Nancy B. Beamer et al. [11] described microalbuminuria as an independent predictor of vascular end point. Meng Lee et al. [12] studied 12 prospective cohort studies with a total of 48596 participants

and 1263 stroke events and found that microalbuminuria was associated with greater risk after adjustment for cardiovascular risk factors. They found that baseline microalbuminuria have a risk of future stroke approximately 90% greater than those without microalbuminuria. P. C. Mathur et al. [13] investigated the incidence, risk factor and severity of stroke with microalbuminuria in nondiabetic ischaemic stroke in Indians (68%).

## 2. MATERIALS AND METHODS

The study was undertaken at SCB Medical College, Cuttack, India during the period from October 2013 to September 2014. Sixty (60) patients with clinical diagnosis of recent ischaemic stroke confirmed by non contrast CT scan of brain were taken for study. Severity of neurological deficit was measured by Scandinavian Stroke Scale. Thirty (30) cases of age and sex matched healthy person were taken as controls. Diabetes mellitus, family history of diabetes, patients with impaired glucose tolerance, previous history of hypertension, case of nephropathy and abnormal urine analysis (glycosuria, haematuria, pyuria, proteinuria), atrial fibrillation, infection, intracranial haemorrhage, neoplasm, females during menstrual period and pregnancy were excluded from study [14].

Microalbuminuria (MA) can be defined as urinary albumin excretion rate of 20-300 mg/L in spot sample or 30-300 mg/24 hrs urine collection or urine albumin creatinine ratio in first voided morning sample is 30-300 micro g/mg [15]. In this study, microalbuminuria was defined as 20-300 mg/L.

Urine samples were taken from morning urination sample within 24 hours of admission. Nephelometric micral assay (immunoprecipitation) was used based on colour shift of polyclonal antihuman antibody (sheep) to human albumin labelled with gold [16], manufactured by Dade Behring, Germany. Analytical sensitivity >95 percent; Analytical specificity >80 percent.

Scandinavian Stroke Scale was used for clinicometric assessment in acute stroke patients. It is a stroke impairment scale evaluates level of consciousness, eye movement, power in

arm, hand and leg, orientation, speech, facial paresis and gait and in total score ranging from 0 to 58. Scandinavian stroke scale is easier than NIHSS for clinical practice in acute stroke patients. Stroke scores below 22 has poor prognosis. It is not used for follow up patients [17,18].

Non contrast CT Scan of Brain was done within 24 hours of occurrence of stroke. Detailed clinical examination, Complete CBC count, urine Routine & microscopic examination, FBS, HbA1C, S creatinine and S. Urea, S. lipid profile, Liver Function Test were also done.

Statistical analysis was performed by using software SPSS version 18.0. The data were expressed as the mean  $\pm$  SD, unpaired student 't' test, Chi square test, 95% confidence limit  $p < 0.05$  was taken as level of significance. Spearman rho correlation was done between MA and score of Scandinavian stroke scale to see the significance of the test.

### 3. OBSERVATION

Over a period of 12 months, 60 recent stroke patients were studied within the age group of 33 to 88 years. Mean age was  $61.1 \pm 13.2$  years. Below 50 years, there were 12(20%) cases and 8 (26.6%) controls. Out of 12 cases, 4(33%) MA positive and 8(66%) MA negative. In age group 51-60 years there were 19(31.6%) cases, out of which 10(52%) were MA positive and 9(48%) were MA negatives. In age more than 60 years, there were 29 cases among them 15(51.7%) were MA positives and 14 (48.3%) MA negatives

and there were 16 controls out of which only 2 (12.5%) were MA positives (Fig. 1).

Out of 60 cases 35(58.3%) were males and 25(41.6%) were females where as in controls 17(56.6%) are males and 13(43.3%) females (Fig. 2).

Among cases 31 (51.6%) had left side hemiparesis, 20 (33.3%) had right hemiparesis, 8 cases (13.3%) had bilateral involvement, and 1 had no focal deficit. In our study group, right ACA infarcts were in 7 cases (11.6%), left ACA infarct 3(5%), right MCA territory infarct 22(36.6%), left MCA 8(13.3%), PCA infarct in 2 (3.3%), lacunar infarct were found in 10(16.6%) and multiple infarcts in 8(13.3%). Predisposing factors were present in 20 cases which include smoking in 12(60%) cases and alcoholics were 8 (13.3%).

Out of 60 cases microalbuminuria was present in 29(48.3%) cases and absent in 31(51.66%) (Fig. 3), where as in controls 3 were (10%) MA positives and 27 (90%) were MA negative (Fig. 4). 95% confidence interval =0.036-0.161, Odd ratio 0.161. Thus patient with recent ischaemic stroke had 4.75 times more possibility of microalbuminuria compared to controls.

Among MA positive cases mean age was  $60.7 \pm 16.3$  and MA negative cases mean age was  $56.47 \pm 13.2$  ( $P=0.437$ ). In MA positive cases males were 16(55.1%) and females were 13(44.8%)  $P=0.238$ . Linear regression curve shows no relationship between age and microalbuminuria (Figs. 5 and 6).

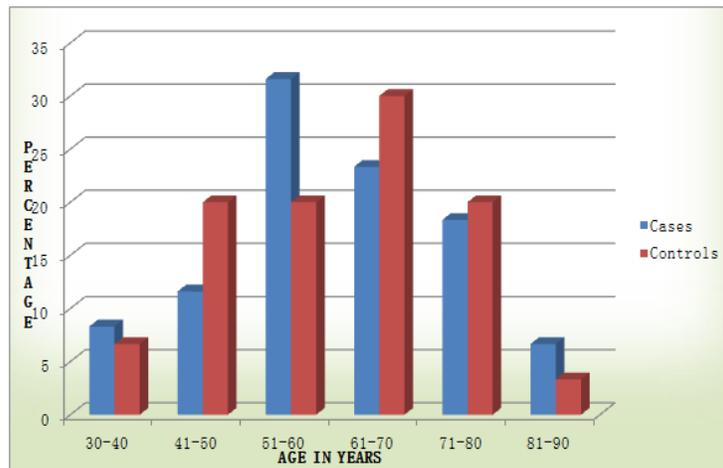


Fig. 1. Age distribution in cases and controls

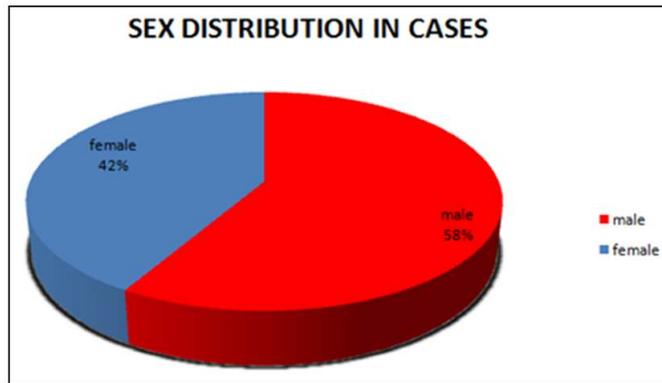


Fig. 2. Distribution of sex among cases

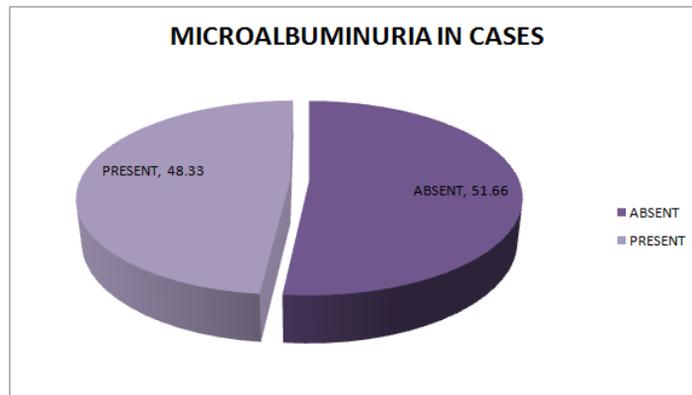


Fig. 3. Microalbuminuria in cases

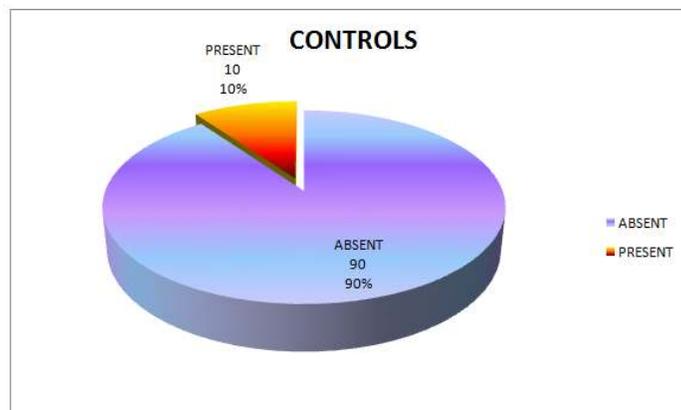


Fig. 4. Microalbuminuria in control

Among cases, mean SBP was  $146 \pm 22.9$  mm of Hg among MA positive and  $143 \pm 19.9$  mm of Hg among MA negative ( $P$  value=0.0547). Serum Cholesterol among MA positives was  $206.3 \pm 38.7$  mg/dl and MA negative  $190.4 \pm 40.3$  ( $P=0.314$ ), S HDL was  $43.4 \pm 7.9$  mg/dl among MA positive

cases and  $42.1 \pm 8.1$  mg/dl in MA negative cases ( $p =0.684$ ), and S creatinine was  $0.88 \pm 0.15$  mg/dl among MA positives and  $0.94 \pm 0.1$  mg/dl among MA negative cases (Table 1). Smoking was present in (8) 27.5% cases of microalbuminuria positives and in (4)12.9% of

MA negative case with p value 0.0436 (Table 2). Alcohol was present in (3)10.2% of MA positive cases and (5)16% MA negative cases.

The severity of stroke was assessed by Scandinavian Stroke Scale was below 22 in 33(55%) cases, between 22-40 in 18 cases(30%)

and more than 40 in 9 cases (15%). Stroke scale was found to be significantly lower in presence of microalbuminuria (mean  $16.06 \pm 9.04$ ) than without microalbuminuria (mean  $22 \pm 12.5$ ) with P value  $< 0.001$ . 95% Confidence Interval 13.68-20.44 in MA positives (Fig. 7).

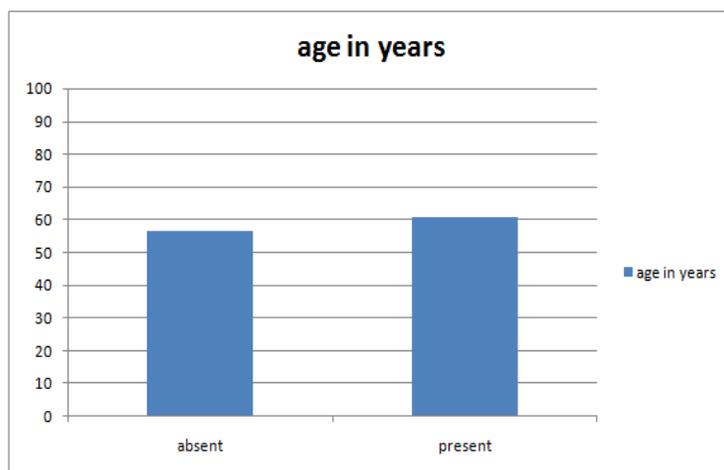


Fig. 5. Association of age with presence of microalbuminuria

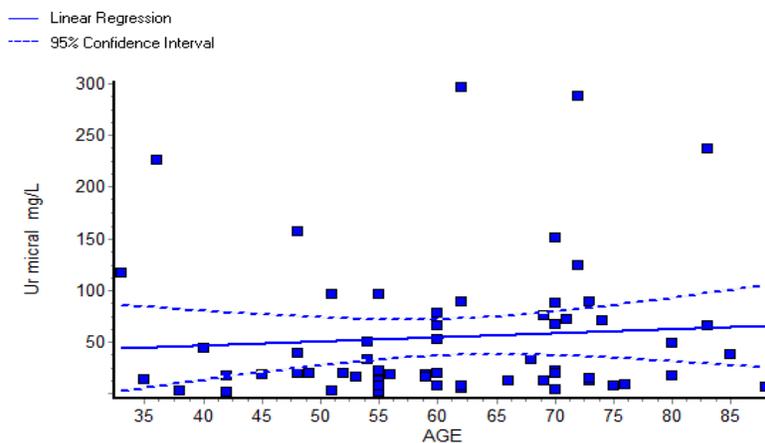


Fig. 6. Association of age with microalbuminuria levels

Table 1. Mean pattern of parameters in cases

	MA +VE cases	MA -VE cases	P value
S. urea	29.2±6.05	25.4±4.7	0.072
S. creatinine	0.88±0.15	0.94±0.1	0.337
S. cholesterol	206.3±38.7	190.4±40.3	0.314
S. HDL	43.4±7.95	42.1±8.1	0.684
S. triglyceride	181.2±54.1	190±79.7	0.749

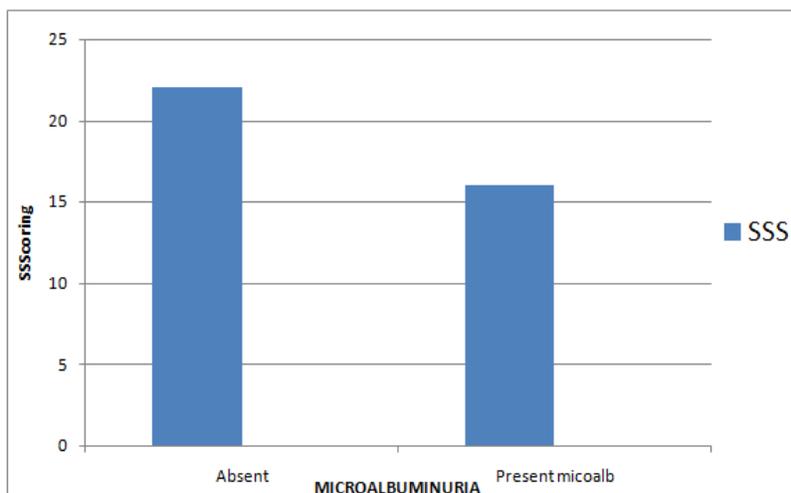


Fig. 7. Mean pattern of SSS in presence of microalbuminuria

Table 2. Predisposing factors

	Cases		Controls	P value
	MA positive	MA negative		
Smoking	8 (27.5%)	4 (12.9%)	7 (23.3%)	0.0436
Alcohol	3 (10.2%)	5 (16%)	3 (10%)	0.0239

#### 4. DISCUSSION

Microalbuminuria has been a marker for monitoring diabetes mellitus for years. In the present study the frequency of microalbuminuria and its correlation with neurological deficit in ischaemic stroke has been demonstrated by cross sectional study in 60 diagnosed ischaemic stroke patients.

It was noted that among cases mean age was 61.1±13.27. Among controls mean age was 59±14.2. Among microalbuminuria positive group mean age was 60.7±16.3 years as opposed by microalbuminuria negative group 56±13.2 years. Among cases below 50 years prevalence was 10.3%, between 50-60 years 27.5%, above 60 years it was 65%. This shows microalbuminuria incidences increases with ages. In study done by J Chowdhary, N Sultana [19] incidence of microalbuminuria was 80% among age more than 60 years, which is similar to our study. According to Beamer et al age is an independent factor for presence of MA in stroke patients [11]. But in our study it may be due to older patients having severity of neurological dysfunction.

Among cases with microalbuminuria positives there was 55.2% were males and 44.8% were

females and in microalbuminuria negatives males are 61.3% and 38.7% females. In both groups microalbuminuria is more common in males but not statistically significant. This was consistent with study by Turaj et al. [20] where male were more with no statistical significance.

Urine microalbumin was tested among age and sex matched cases and controls showed recent stroke have 4.75 times more incidence of microalbuminuria in cases compared to control groups. Incidence of microalbuminuria among ischaemic stroke cases were 48.3% and among controls 10% with 95% CI was 0.360-0.161. Interestingly a similar high prevalence of microalbuminuria in stroke patients was observed by Beamer et al. [11] where microalbuminuria was present in 30% of stroke patients and 10% of controls matched for stroke risk factors. Turaj et al. [10] found 46.1% incidence of microalbuminuria in acute non diabetic ischaemic stroke as opposed to only 13.5% controls. In another study by Slowik et al. [10] microalbuminuria was found in 46.7% of acute ischaemic stroke patients, 16.5% of subjects with history of stroke and 16.7% of healthy control<sup>3</sup>. With reference to study done by Muhammed Ahsan et al. [21] in Pakistan,

microalbuminuria incidence was 48.2% with mean value  $63.54 \pm 6.6$ .

Prevalence of microalbuminuria in different subtypes of infarction were 50% in MCA infarct, 16.7% in ACA infarct, 3.3% in PCA infarct, lacunar infarcts in 16.6% and combination of territories in 13.3%. Here microalbuminuria did not differ among major sub types of stroke. According to Beamer prevalence of microalbuminuria did not differ among major sub types of strokes [11] and after adjusting diabetes, hypertension microalbuminuria was weakly prognostic, however in patients with history of transient ischaemic attack, recent and remote stroke it was an independent marker for future attack [11].

Analysing association of presenting symptoms with microalbuminuria, loss of consciousness was present in 68% of patients with microalbuminuria compared to 32% MA negative cases. According to Turaj et al. [10] patients with microalbuminuria, loss of consciousness was associated in 35.5% cases. This may be the fact that the severity of cases was more in our group of patients.

It has been studied that MA in general population correlates with factors that increase atherosclerosis i.e high blood pressure, high triglyceride, low HDL, increased carotid intima thickness [22]. S. urea, S. creatinine, S. lipid profile were found similar in cases and controls and not statistically significant. According to Arboix et al. [14] atrial fibrillation is an independent risk factor of microalbuminuria, associated with higher in-patients mortality in ischaemic stroke patients, but in our study atrial fibrillation has been excluded. Mykkanen et al. [23] studied 1449 patients and found that higher prevalence of MA in diabetic than non diabetics (27.6% vs 13.9%). In present study we excluded diabetes mellitus in order to obtain group of patients without additional risk of cardiovascular death.

Comparing Scandinavian Stroke scale with microalbuminuria within 24 hours of onset of stroke, patients with MA scored lower than without MA. In present study Scandinavian Stroke score  $16.9 \pm 9.04$  (range 1-30), 95% CI =17.3, P = 0.001 as compared to MA negative  $22.1 \pm 12.5$  (range 2-47) showing that microalbuminuria incidence increases with severity of stroke. In study by Turaj et al. [10] MA positive Scandinavian Stroke Score 26 and in

MA negative Scandinavian Stroke is score 39 which share similar view.

Meta-analysis by Meng Lee et al. [12] have highlighted that stroke risk might get reduced when microalbuminuria incidence is reduced, which can be achieved through angiotensin receptor blocker or ACE inhibitors. As the prevalence of MA ranged from 12-40% in population it is cost effective to screen and reduce cerebrovascular events.

## 5. LIMITATIONS

Our study has some limitations. Our study did not have consecutive recruitment of patients and numbers of patients included were relatively small. Moreover, as the study was cross sectional in design, it is not easy to predict exactly whether MA preceded stroke or vice versa. Future cohort studies with large samples will be helpful in providing an answer.

## 6. CONCLUSION

Microalbuminuria increases the ischaemic stroke risk because of association between microalbuminuria with carotid intima media thickness and reflecting increased vascular endothelial permeability leading to endothelial dysfunction. The present study found microalbuminuria in 48.33% non diabetic nonhypertensive ischaemic stroke and degree of MA increases with severity of stroke. Hence it is important to screen high risk patients for microalbuminuria on regular basis. Limiting urinary albumin excretion with angiotensin receptor inhibitor may reduce vascular events including stroke beyond blood pressure lowering effect. Moreover interventional trials are needed to establish whether the correction of increased urine albumin excretion rate in its own right modifies the risk of adverse vascular events.

## CONSENT

All authors declare that written informed consent was obtained from the patients for study.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Hankey GJ. Stroke: How large a public health problem and how can the neurologist help: Arch Neurol. 1999;56:748-54.
2. Fiona C. Taylor, Suresh Kumar K. Stroke in India factsheet (updated 2012).
3. Basi Seema, Albert Mimran, Pierre Fesler, Julia B Lewis. Microalbuminuria in type 2 diabetes and hypertension. A marker treatment target or innocent bystander? Diabetes Care. 2008;31:194-201.
4. Gosling P, Hughes EA, Reynolds TM, Fox J. Microalbuminuria is an early response following acute myocardial infarction. Eur Heart J. 2001;12:508-13.
5. Ochodnický P, Henning RH, Van Dokkum RP, De Zeeuw. Microalbuminuria and endothelial dysfunction: Emerging targets for primary prevention of end organ damage. J Cardiovasc Pharmacol 2006;47(Supple 2):S151-62.
6. Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, Kofoed. Albuminuria reflects widespread vascular damage. The Steno Hypothesis. Diabetologia. 1989; 32:219-26.
7. Davignon J, Ganz P. Role of endothelial dysfunction in atherosclerosis. Circulation. 2004;109:27-32.
8. Mykkänen L, Zaccaro DJ, O'Leary DH, Howard G, Robbins DC, Haffner SM: Microalbuminuria and carotid artery intima media thickness in nondiabetic and NIDDM subjects. The Insulin Resistance Atherosclerotic Study (IRAS). Stroke. 1997;28:1710-16.
9. Gumbinger C, Sykora M, Diedler J, Ringeb P, Rocco A. Microalbuminuria: A potential prognostic marker for acute stroke. Nervenarzt. 2012;83(10):1357-60.
10. Slowik A, Turaj W, Iskra T, Strojny J, Szczudlik A. Microalbuminuria in nondiabetic patients with acute ischaemic stroke: Prevalence, clinical correlates and prognostic significance. Cerebrovascular Disease Basel Switz. 2002;14(1):15-21.
11. Beamer NB, Coull BM, Clark WM, Wynn M. Microalbuminuria in ischaemic stroke. Arch Neurol. 1999; 56(6):699-702
12. Lee M, Saver JL, Chang KH, Liao HW, Chang SC, Ovbiagele B. Impact of microalbuminuria on incident stroke: A meta analysis. Stroke J Cerebral Circulation. 2010;41(11):2625-31.
13. Mathur PC, Punekar Prashant, Muralidharan R. Microalbuminuria in Nondiabetic Acute Ischaemic Stroke-An Indian Perspective Annals Indian Academy of Neurology. 2005;1,8(4):237-42.
14. Arboix A, Garcia Eroles L, Mansson JB, Oliveres M, Panjades R, Targa C. Atrial fibrillation and stroke: Clinical presentation of cardioembolic versus atheroembolic infarction. Int J Cardiol. 2000;73:33-42.
15. David BS. Carbohydrate. In: Burtis HC, Ashwood RE, editors. Tietz text book of clinical chemistry. 3<sup>rd</sup> ed: Philadelphia: Saunders. 1999;798-801.
16. Toto RD. Microalbuminuria: Definition, detection and clinical significance. J Clin Hypertension. 2004;1(6):2-7.
17. Scandinavian stroke study group. Multicentre trial of hemodilution in ischaemic stroke: Background and study protocol. Stroke. 1985;16:885-90.
18. Luvizotto Gustavo J, Gabriel Maicon Goncalves, Gabriel Pariera Braga, Thiago Dias Fernandes. Aspects correlates with Scandinavian stroke scale for predicting early neurological impairment. Arquivos de Neuro-Psiquiatria. 2015;73(5).
19. Chowdhury J, Sultana N, Ahmed S, Rahman M, Akter M, Rafique T. Microalbuminuria as predictor of short term mortality in acute ischaemic stroke. Bangladesh Journal Medical Biochem. 2012;5(1):16-19.
20. Turaj W, Slowik A, Wyrwicz-Petkow U, Pankiewicz J, Iskra T, Rudzinska M, Szczudlik A. The prognostic significance of microalbuminuria in non-diabetic acute stroke patients. Med Sci Monit Int Med J Exp Clin Res. 2001;7(5):989-94.
21. Muhammad Ahsan F, M Sohail Anjum, Malik Fayyaz A, Naila Kalsoom. Frequency of Microalbuminuria in patients with ischaemic stroke. Rawal Medical Journal. 2013;38(2):97-98.
22. Haffner SM, Stern MP, Gruber KK, Hazuda MP, Mitchell BD, Patterson JK. Microalbuminuria. Potential marker for

- increased cardiovascular risk factors in non diabetic subjects? *Atherosclerosis*. 1990;10:727-31.
23. Mykkanen L, Zaccaro DJ, O'Leary DH, Howard G, Robbins DC, Haffner SM. Microalbuminuria and carotid intima-media thickness in nondiabetic and NIDDM subjects. The Insulin Resistance Atherosclerosis Study (IRAS). *Stroke*. 1997;28:1710-1716.

---

© 2016 Pattanaik and Dash; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*  
*The peer review history for this paper can be accessed here:*  
<http://sciedomain.org/review-history/13953>