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Association of Microalbuminuria with Ischemic Stroke among Patients Admitted in a Tertiary Health Care Hospital in North India

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ABSTRACT

Background: Microalbuminuria defined as urinary albumin excretion of 30-300 mg/24hrs is considered a marker of vascular endothelial damage and thereby of atherosclerosis; which is cornerstone of the pathogenesis of ischemic stroke. The present study was done to highlight the association of microalbuminuria with ischemic stroke.

Methods: This was an institution based study conducted over a period of one year at GMC Jammu. It consisted of 100 ischemic stroke patients fulfilling inclusion criteria. The severity of stroke was assessed by NIHSS score and urine for albumin was estimated by chemiluminescence technique.

Results: Out of 100 patients, 47% (47out of 100) had microalbuminuria and 51% didn't have. Mean NIHSS score of patients with microalbuminuria was 21.8 ± 9.42. Mean albumin excretion amongst mild stroke patients was 36 ± 2.77 and in severe stroke was 147.38 ± 26.3. As the albumin excretion increased, the severity of stroke in terms of NIHSS also increased. Thus, a graded correlation existed between severity and amount of albumin excretion among microalbuminurics. This correlation was highly significant with correlation coefficient of 0.904 and p value of <0.0001. No graded correlation existed between severity of stroke in terms of NIHSS and albumin excretion below the range of microalbuminuria.

Conclusion: Microalbuminuria was found in significant number of ischemic stroke patients and was independently associated with adverse outcomes in terms of severity of stroke.

Keywords: Ischemic Stroke, Microalbuminuria, NIHSS score

INTRODUCTION

Stroke as defined by WHO is "rapidly developing clinical signs of focal(at times global) disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death ,with no apparent cause other than of vascular origin." [1] In 2013, globally, approximately 6.9 million people had an ischemic stroke and 3.4 million people had a hemorrhagic stroke (Global Burden of Disease, 2013) In 2015, stroke was the second most frequent cause of death after coronary artery disease, accounting for 6.3 million deaths out of which 3.0 million deaths resulted from ischemic stroke while 3.3 million deaths resulted from hemorrhagic stroke (Global Burden of Disease, 2015). [2] Overall, two-thirds of stroke occurred in those over 65 years old. [3] Stroke is a medical emergency and the sooner it is diagnosed and treated, the better the outcome. It is vital to distinguish between a stroke and conditions that may present as a stroke. Validated formal screening tools are used to assist with the rapid diagnosis of a stroke. The two most commonly used are FAST (an acronym for face, arm, speech, time) and ROSIER (Recognition of stroke in emergency room) [4]

Microalbuminuria(MA) is defined as urinary albumin excretion of 30 to 300mg/24 hrs or urinary albumin creatinine ratio(UACR) in the first voided sample in the morning(clean, midstream) greater than 30-300mg/g [5] or early morning urine albumin concentration of 20-200mg/L. [6] It is considered as a marker of vascular endothelial damage, the latter being the underlying cause of vascular diseases [7] and may be related to vascular damage by several biological pathways like renal dysfunction, transvascular escape of albumin, endothelial dysfunction or inflammation. [8]

There is close relation between atherosclerosis, endothelial dysfunction and leakage of protein through glomerulus. Endothelial dysfunction(ED) can be considered when endothelial properties have changed in a way that is inappropriate with regard to the preservation of organ function. In ED most endogenous potent vasodilator Nitric Oxide production or its activity is hampered which leads to arterial vasoconstriction. This causes increased arterial as well as glomerular pressure and permeability. In ED, glomerular basement membrane loses its normal negative charge. [9] It also causes loss of surface heparin like proteoglycan molecules that prevent thrombus formation and smooth muscle growth thus promoting thrombus formation and intimal thickening which enhance atherosclerosis .So in ED both atherosclerosis and microalbuminuria are found. Most of the acute ischemic stroke happened due to atherosclerosis by sudden occlusion of the lumen developed by the superimposed thrombosis or haemorrhage into atheroma. [10] Hence microalbuminuria reflects generalized vascular damage that means ED and is an early marker of atherosclerosis**.** [11]

MATERIALS AND METHODS

A minimum of 100 cases were taken. Cases were selected from the patients admitted in the Department of Medicine, Government Medical College, Jammu over a period of one year with diagnosis of ischemic stroke fulfilling the inclusion and exclusion criteria. The study was done after approval from ethical committee. The severity of stroke was assessed by NIHSS (National Institute of Health Stroke Scale) at the time of admission and urine for albumin was estimated. Urine for albumin was estimated by quantitative estimation of urinary protein by biochemistry analyser using Electrochemiluminescence (ECL) technique.

NIHSS (National Institute of Health Stroke Scale): [12]

It is a tool used by healthcare providers to objectively quantify the impairment caused by stroke. The NIHSS is composed of 11 items, each of which scores a specific ability between 0 and 4.For each item, a score of 0 typically indicates normal function in that specific ability, while higher score is indicative of some impairment. The maximum possible score is 42 with the minimum score being 0.

INCLUSION CRITERIA

- Age more than 30 years
- Ischemic stroke patients who presented within 24 hours of onset of acute ischemic stroke as confirmed by CT (Computed Tomography) and/ or MRI (Magnetic Resonance Imaging).
- Patients with ischemic changes with no hemorrhagic changes on radioimaging.

EXCLUSION CRITERIA

- Patient and attendants who didn't give consent
- Those with established;
  - kidney disease
  - diabetes mellitus
  - chronic inflammatory disease
  - Urinary tract infections
  - Dyslipidemia
  - History of coronary artery disease
  - Transient ischemic attack

STATISTICAL TEST

Categorical variables were presented in number and percentage (%) and continuous variables were presented as

mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used.Quantitative variables were compared using Independent T test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups and Kruskal Wallis test was used for comparison between more than two groups. Qualitative variables were correlated using Chi-Square test/Fisher's Exact test. A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

RESULTS AND DISCUSSIONS

Out of 100 patients, 47(47%) had microalbuminuria and 53(53%) didn't (Fig 1)

Table 1: Distribution of patients of Ischemic stroke with microalbuminuria

Ischemic Stroke	Total patients(n=100) No.(%)
With microalbuminuria	47(47)
Without microalbuminuria	53(53)
Total	**100(100%)**

Amongst those with microalbuminuria 35(35/47=74.9%) were males and 12(12/47=25.53%) were females. Those who did not have microalbuminuria 38(38/53=71.6%) were males and 15(15/53=28.3%) were females. Out of 100 patients of ischemic stroke, 73(73%) were males and 27(27%) were females **(Fig 2).** Among 73 male ischemic stroke patients, 35(47.95%) were having microalbuminuria and 38(52.05%) were not having. Among 27 female ischemic stroke patients, 12(44.44%) were having microalbuminuria and 15(55.56%) were not having (**Fig 3).**

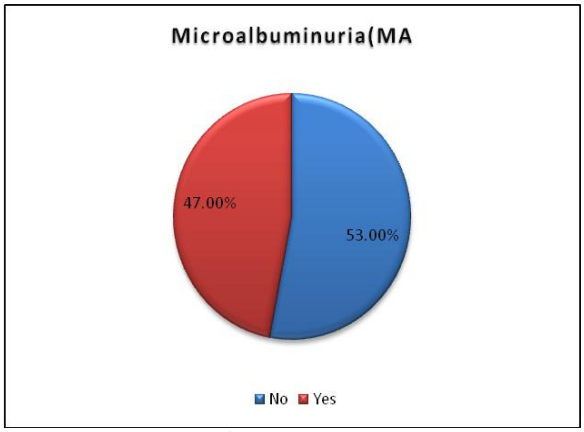

Fig1: Distribution of Ischemic stroke patients with MA

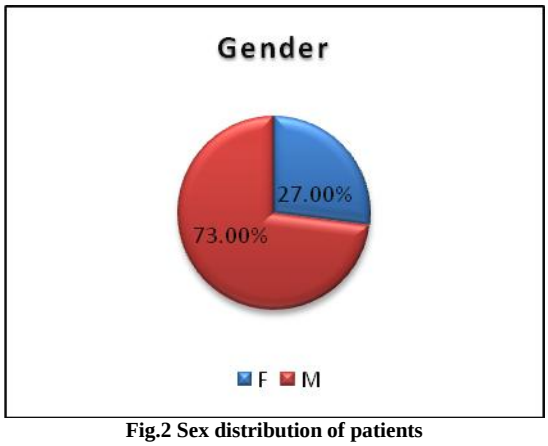

Fig.2 Sex distribution of patients

Table 2: Distribution of patients according to their sex

Sex	Patients of ischemic stroke with microalbuminuria (n=47)(%)	Patients of ischemic stroke without microalbuminuria (n=53)(%)	Total
Male	35(47.95%)	38(52.05%)	73(100%)
Female	12(44.44%)	15(55.56%)	27(100%)
Total	47(47.00%)	53(53.00%)	100(100%)

P value=0.755

Most patients of ischemic stroke belonged to 61-70 years age group(35%).Patients of ischemic stroke with microalbuminuria were mostly in 71-80 years age group(15/47=31.9%); while most patients without microalbuminuria belonged to 61-70 years age group (23/53=43.39%)(**Table3**). Mean age of ischemic stroke patients was 67.35 ± 11.7 with median of 68 years; minimum age being 35 years and maximum age 90 years**(Table 4**). Mean age of patients of ischemic stroke with microalbuminuria was 68.51 ± 12.81 with median of 70 years and that of patients without microalbuminuria was 66.32 ± 10.63 with median of 66 years(**Fig 5**).

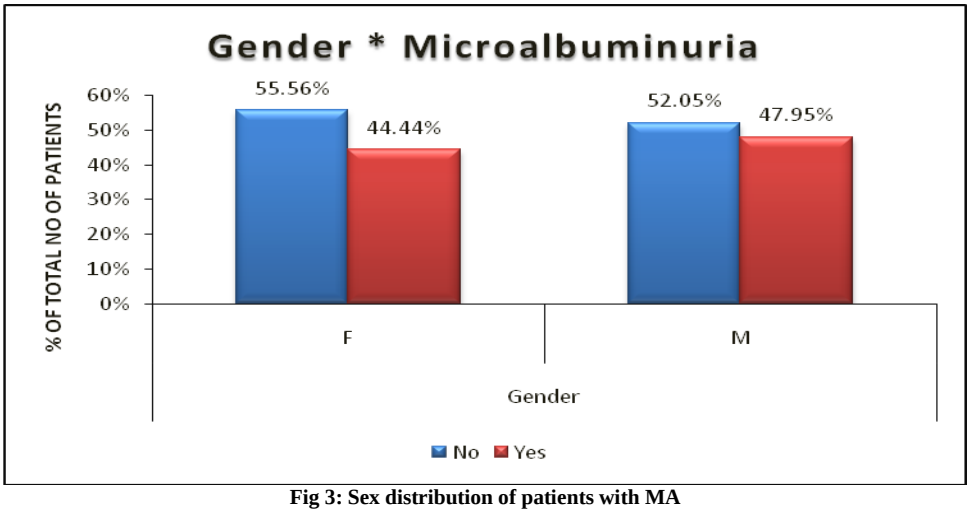

Fig 3: Sex distribution of patients with MA

Table 3: Distribution of patients of ischemic stroke according to their age

Age group (in years)	Patients of ischemic stroke with microalbuminuria n = 47(%)	Patients of ischemic stroke without microalbuminuria n = 53(%)	Total
<40	3(75.00%)	1(25.00%)	4(100%)
41-50	1(16.67%)	5(83.33%)	6(100%)
51-60	9(47.37%)	10(52.63%)	19(100%)
61-70	12(34.29%)	23(65.71%)	35(100%)
71-80	15(60.00%)	10(40.00%)	25(100%)
81-90	7(63.64%)	4(36.36%)	11(100%)
Total	47(47.00%)	53(53.00%)	100(100.00%)

X^2 =8.666 p=0.123

Table4: Mean age of stroke patients

Age	Ischemic stroke patients with microalbuminuria	Ischemic stroke patients without microalbuminuria
Sample size	47	53
Mean± S.D	68.51 ± 12.81	66.32 ± 10.63
Median	70	66
Min- Max	35-90	45-85
Interquartile Range	60-76.5	60-72.75

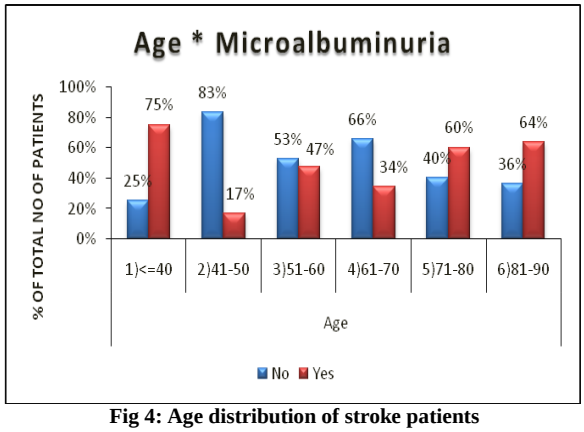

Fig 4: Age distribution of stroke patients

Mean albumin excretion in 100 stroke patients was 61.31 ± 59.02.Mean albumin excretion amongst patients with microalbuminuria in mild stroke was 36±2.77, in moderate stroke was 81.4±24.37, in moderate to severe stroke 97.31±22.07, in severe stroke 147.38±26.3 **(Fig 7**). Mean albumin excretion amongst patients without microalbuminuria in mild stroke was 12.8±4.54, in moderate stroke was 11.69±6.98, in moderate to severe stroke was 20.7±4.22 and in severe stroke was 13.35±5**(Fig 8**). Mean quantity of albumin excretion who were microalbuminurics was 114.68±44.25 and mean quantity of albumin excretion who were normoalbuminurics was 13.98±6.47 (**Fig 6**)

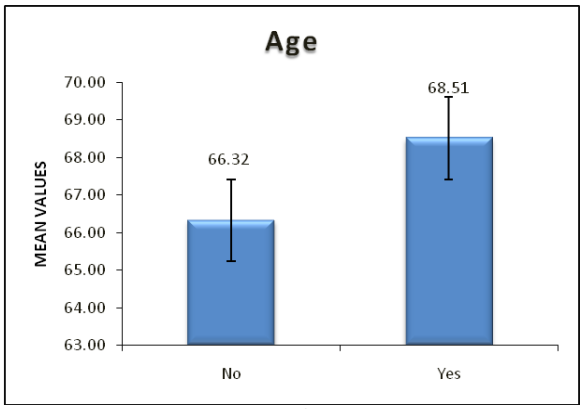

Fig 5: Mean Age of stroke patients

Out of 100 patients, 15(15%) had minor stroke, 26 (26%) had moderate stroke, 23(23%) had moderate to severe stroke and 36 (36%) had severe stroke (**Table 5**). In ischemic stroke patients with moderate to severe stroke, greater percentage belonged to those having microalbuminuria than those who did not have (56.52% vs 43.48%) In ischemic stroke patients with severe stroke, greater percentage belonged to those with microalbuminuria than those who didn't have (66.67% vs 33.33%)(**Table5**). Percentage of patients having microalbuminuria had increased severity of stroke than those who didn't have. This association of severity of stroke with microalbuminuria was significant (p value = 0.001**) (Table5**). Also there existed a graded correlation between severity of stroke and amount of albumin excretion in the range of microalbuminuria. This correlation was highly significant with correlation coefficient of 0.904 and p value of <0.0001(**Fig 9**). Hence severity of stroke correlated with microalbuminuria. Mean NIHSS score of stroke patients with microalbuminuria (21.08±9.42) was greater than mean NIHSS score of patients without microalbuminuria (14.43±8.34). This association was highly significant with p value of 0.0003(**Table 6**). Mean quantity of albumin excretion among total ischemic stroke patients was 61.31±59.02 with median of 25.Mean quantity of albumin excretion who were albuminurics was 114.68±44.25 and in normoalbuminurics was 13.98±6.47(**Fig6)**

Table 5 : Distribution according to severity of stroke using NIHSS

NIHSS	Ischemic stroke patients with microalbuminuria	Ischemic stroke patients without microalbuminuria	Total
Minor stroke	5(33.33%)	10(66.67%)	15(100.00%)
Moderate stroke	5 (19.23%)	21(80.77%)	26(100.00%)
Moderate to severe stroke	13(56.52%)	10(43.48%)	23(100.00%)
Severe stroke	24(66.67%)	12(33.33%)	36(100.00%)
Total	47(47.00%)	53(53.00%)	100(100.00%)

X^2 =15.600 p value=0.001, df= 3

Table 6: Distribution of mean NIHSS score among stroke patients

NIHSS	Ischemic stroke patients with microalbuminuria	Ischemic stroke patients without microalbuminuria
Sample size	47	53
Mean±S.D	21.08± 9.42	14.43±8.34
Median	21	14
	2-39	2-32
Interquartile range	16.250-28	8-20

P value =0.0003

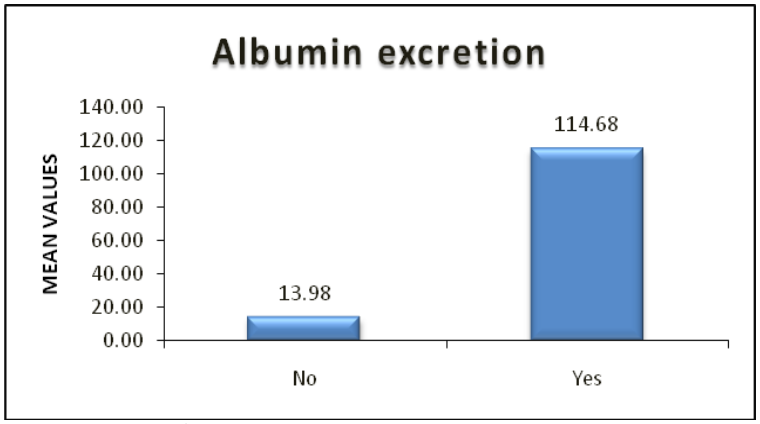

Fig 6: Mean value of albumin excretion among albumin excretors and nonexcretors

Table 7: Distribution of quantity of albumin excretion

Quantity of Albumin excretion	With microalbuminuria	Without microalbuminuria
Sample size	47	53
Mean± SD	114.68±44.25	13.98± 6.47
Median	110	15
Min-Max	33-188	1.2-29
Interquartile range	86.250-149	8.975-20

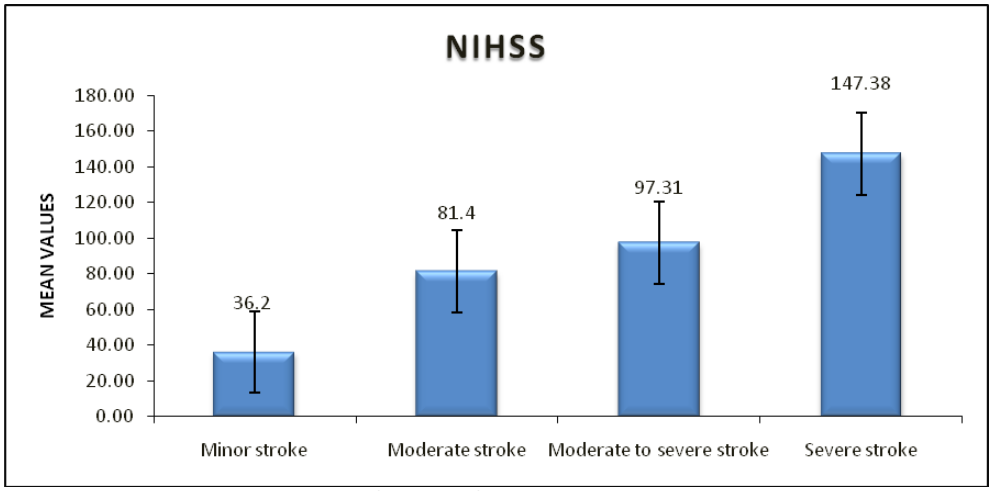

Fig 7: Distribution of severity of stroke amongst microalbuminurics

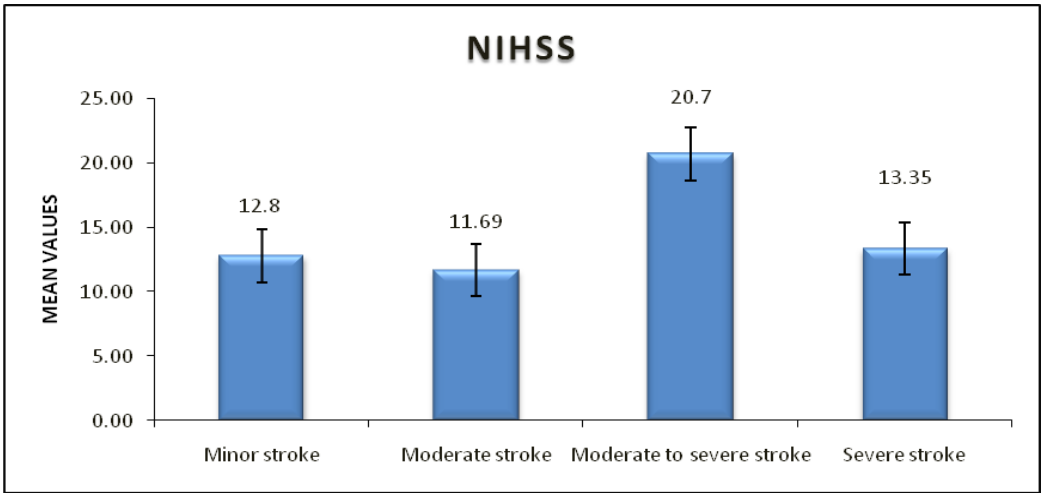

Fig 8: Distribution of severity of stroke amongst normoalbuminurics

Table 8: Table showing correlation of albumin excretion between NIHSS and microalbuminurics

		NIHSS
Albumin excretion	Correlation coefficient	0.904
	p value	<0.0001
	n	47

Table 9: Correlation of albumin excretion between normoalbuminurics and NIHSS

		NIHSS
Albumin excretion below in normoalbuminurics	Correlation coefficient	0.191
	p value	0.1707
	n	53

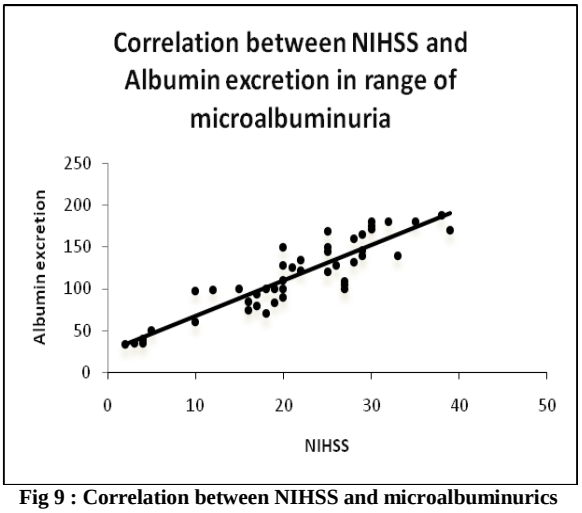

Fig 9 : Correlation between NIHSS and microalbuminurics

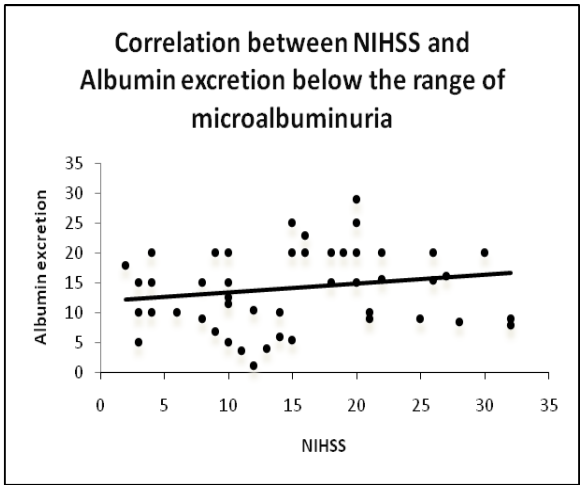

Fig 10: Correlation between NIHSS and normoalbuminurics

No graded correlation existed between severity of stroke in terms of NIHSS and albumin excretion below the range of microalbuminuria as was there between microalbuminurics and severity. This correlation is not significant with p value of 0.1707 and correlation coefficient of 0.191(**Fig 10)**

CONCLUSION:

Microalbuminuria is found in large percentage of patients with ischemic stroke and is independently associated with adverse outcome in terms of severity of stroke. Higher the albumin excretion, more is the severity of stroke i.e. NIHSS and vice versa.

As microalbuminuria assessment is a simple, clinical test that is readily available Therefore, its measurement may help to assess those who are at increased risk and to triage those who may need a more aggressive management protocol.

Conflicts of Interest: None

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