

STUDY OF RENAL FUNCTION TESTS IN PATIENTS OF ACUTE HAEMORRHAGIC STROKEAditya Vardhan Singh¹, Harsh Vardhan Singh², Shreshtha Singh³**HOW TO CITE THIS ARTICLE:**

Aditya Vardhan Singh, Harsh Vardhan Singh, Shreshtha Singh. "Study of Renal Function Tests in Patients of Acute Haemorrhagic Stroke". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 38, May 11; Page: 6649-6663, DOI: 10.14260/jemds/2015/963

ABSTRACT: OBJECTIVE: To study renal function tests in patients with acute haemorrhagic stroke and to find association of abnormal renal function with adverse outcome in patients with acute haemorrhagic stroke. **MATERIAL AND METHODS:** The study was conducted at Darbhanga Medical College & Hospital, Laheriasarai, Darbhanga during the period from January 2012 to September 2013. This was an observational study. A total of 100 patients presenting with acute haemorrhagic stroke admitted to the hospital or reporting in OPD/Emergency for stroke were included in this study after having taken written informed consent. Cases were selected by random sampling. **OBSERVATION:** Out of 100 patients with acute haemorrhagic stroke 92 patients had intracerebral haemorrhage and 8 patients had subarachnoid haemorrhage. Patients were divided into two groups on the basis of estimated glomerular filtration rate (eGFR). Group A (eGFR >60 ml/min/1.73 m² BSA) comprised of 71% of total stroke patients and group B (eGFR <60 ml/min/1.73 m² of BSA) consisted of 29% of total stroke patients. Out of 71 patients in group A, 14 (19.72%) patients died within 30 days of presentation and out of 29 patients in group B, 8 (27.58%) patients died within 30 days. Out of 22 patients who died within 30 days of presentation 14 (63.60%) had serum creatinine >98 μmol/L and 15 (68.60%) patients had blood urea >6.8 mmol/L. **CONCLUSION:** This study clearly indicated that renal dysfunction as evidenced by (a) eGFR <60 ml/min/1.73 m² of BSA, b) Sr creatinine >98 μmol/L & c) Blood urea >6.8 mmol/L, are not only an important risk factor for acute haemorrhagic stroke but are also an independent predictor of mortality within 30 days of presentation.

KEYWORDS: Intracerebral haemorrhage, subarachnoid haemorrhage, estimated glomerular filtration rate (eGFR), serum creatinine, blood urea.

INTRODUCTION: Stroke is a major cause of mortality and morbidity worldwide. It is the 2nd commonest cause of death and one of the most important cause of disability (Strong 2007).¹

In India about 90-220 patients per lacs have been observed (Dalal 2007).² There are about 1.44-1.64 x 10⁶ cases of new stroke every year (WHO 2005).³

Acute Haemorrhagic stroke is the largest killer apart from Ischemic Stroke. Cases of haemorrhagic stroke frequently presents as a bolt from the blue. Sudden loss of consciousness, vomiting, convulsion and loss of function in ½ of body or a limb is the common presentation. Although patient may remain conscious and present with any of the above symptoms. Hypertension has been observed as one of the commonest association of stroke. But in many cases blood pressure (BP) may be low or normal or there is only isolated systolic hypertension or truncated hypertension. Vascular malformations, aneurysms and various types of angiopathies may be associated with stroke mainly Sub-arachnoid haemorrhage.

Early stroke survivors have been followed and investigation showed raised serum creatinine concentration in them (Friedman et al).⁴ When followed for a period of 18 months by this author, it

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was observed that mortality was higher in those patients who had higher serum creatinine concentration. Mc Walter et al,⁵ showed in a larger group of acute stroke patients that mortality was higher among patients with reduced renal function on admission.

In a subsequent study known as Northern Manhattan Study (NOMAS),⁶ which followed 3298 stroke-free subjects for a mean follow-up time of 6.5 years for vascular outcomes. This study showed that renal failure patients with GFR levels of between 15 and 59mL/min are at a high risk for stroke. Moreover, impaired kidney function has been associated with cerebral micro-bleeding. The incidence of stroke and associated mortality is also higher in kidney disease patients compared with the general population.

The present study is aimed to assess the renal function test in patients of acute haemorrhagic stroke. The study will also include finding out any association of adverse outcome with abnormal renal function in these patients.

AIMS AND OBJECTIVE:

1. To study renal function tests in patients with acute haemorrhagic stroke.
2. To find association of abnormal renal function with adverse outcome in patients with acute haemorrhagic stroke.

MATERIAL AND METHODS: The present study was conducted at Darbhanga Medical College & Hospital, Laheriasarai, Darbhanga during the period from January 2012 to September 2013. This was an observational study to find the association of renal dysfunction in acute haemorrhagic stroke and to assess adverse outcome in terms of mortality.

A total of 100 patients presenting with acute haemorrhagic stroke admitted to the hospital or reporting in OPD/Emergency for stroke were included in this study after taking informed consent. Cases were selected by random sampling.

SELECTION CRITERIA OF CASES:

Inclusion Criteria: Patients above 18 years of age presenting with clinical diagnosis of acute haemorrhagic stroke, later confirmed by CT scan / MRI were included in the study.

Exclusion Criteria: Cases with following factors were excluded from the study groups: -

1. Head injury.
2. Metastasis.
3. Bleeding disorder.
4. Primary SOL (space occupying lesion).
5. On anticoagulation therapy.
6. Patients with acute kidney injury.

On the basis of CT SCAN haemorrhagic stroke was further categorised as one of the two broad pathological types:

1. Intracerebral haemorrhage.
2. Subarachnoid haemorrhage.

METHODS OF DATA COLLECTION: Patient details were recorded as regards:

1. Age
 - Age of the patient divided into three groups as follows:
 - I. 18-40 years.
 - II. 40-65 years.
 - III. 65 years.
2. Sex of the patient.
3. Complaint of the patient.
4. History of diabetes, hypertension, alcohol consumption, smoking/nicotine use, drug use, trauma, past history of TIA/stroke, cardiovascular disease or any other medical illness. Family history of diabetes, hypertension, stroke, cardiovascular disease.
5. Detailed clinical examination for vital parameters and neurological deficit were done for of all patients as per Performa. In all patients at admission Glasgow coma scale scoring was done.
6. Following investigations were done:
 - CTscan head.
 - Hb%TC, DC, ESR.
 - Complete Haemogram.
7.
 - BT, CT, PT, aPTT, Platelet count.
 - Routine and microscopic examination of urine.
 - RBS, Blood urea & Serum Creatinine Serum Electrolytes.
 - Lipid profile.
 - ECG.

Other Investigations Like: Chest X-Ray, MRI, Echocardiography, liver function tests, connective tissue workup are done whenever needed.

- Renal function on admission was assessed using the abbreviated equation of the

Modification Diet for Renal Disease (MDRD) that estimates the glomerular filtration rate (eGFR) from the following formula:

$$\text{eGFR (in ml/min per 1.73m}^2\text{)} = 186.3 \times P \text{ cr (e}^{-[1.154]} \text{) x.}$$

$$\text{Age (e}^{-[0.203]} \text{) } \times (0.742 \text{ if female) } \times (1.21 \text{ if black).}$$

Since the use of the MDRD formula requires that renal function is in a steady state, patients with acute kidney injury (AKI) were identified and excluded from the study. The absolute or relative change in serum creatinine was used to define AKI [absolute increase in serum creatinine of either ≥ 0.3 mg/dl (≥ 25 $\mu\text{mol/l}$) or a percentage increase of $\geq 50\%$, on the basis of the ADQI definition].

Patients were divided into two groups on the basis of eGFR:

Group A comprised patients with eGFR >60 ml/min/1.73 m² of body surface area (BSA).

Group B comprised patients with eGFR <60 ml/min/1.73 m² of BSA.

Hypertension: Blood pressure was taken at the time of admission and at the time of discharge and those who had systolic BP >140 mmhg and diastolic BP >90 mmhg were considered as hypertensive.

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Patients who were treated for hypertension before stroke were also considered to have hypertension. Patients with stroke who had transient hypertension resulting from increased intracranial pressure (Cushing reflex) who did not receive anti-hypertensive treatment at the time of dismissal were not considered to have hypertension.

Diabetes Mellitus: Diabetes mellitus was considered present when subjects gave history of diabetes mellitus and were on diet/oral hypoglycemic drugs or received insulin treatment or had random blood sugar >200mg/dl with complications of diabetes, fasting plasma glucose of more than 126mg/dl, post prandial blood glucose more than 200mg/dl or HbA1c more than 6.5%.

Dyslipidemia: Dyslipidemia was defined when a patient had a diagnosis of it and/or was on diet or lipid lowering agents or had fasting blood cholesterol >200mg/dl, triglycerides > 180mg/dl, LDL > 100mg/dl during hospital stay.

Cardiovascular Causes: Patients were considered to have a cardiac abnormality when they had a self-reported history of myocardial infarction, coronary artery bypass grafting, angina or percutaneous transluminal angioplasty. The 12 lead ECG of each patient was recorded. The presence of high QRS voltage i. e. sum of S wave in V1 lead and R wave in V5 or V6 lead of 35 mm or more was considered evidence of left ventricular hypertrophy. ECG evidence of possible or definite myocardial ischemia i. e. 1mm depression of ST segment or myocardial infarction by presence of Q/QS pattern was noted and atrial fibrillation if any was documented.

Obesity: Obesity was defined as patient with BMI > 30 kg/sqm.

Initially all patients were treated conservatively with anti-cerebral edema measures which comprised of: Mannitol 1gm/kg in three divided doses/day, followed by oral glycerol 30 ml three times a day. Those patients whose blood pressure was high were treated with antihypertensive agents appropriate to degree of hypertension. All patients received injectable antibiotics and antacids as prophylaxis against gastric bleed. Nutrition was maintained in all unconscious patients by nasogastric feeding. Vigorous respiratory care and physiotherapy was instituted in all patients' right from the time of admission.

Outcome in stroke patients was assessed in terms of mortality.

At the end of the study, the data collected were compiled, tabulated and analyzed by means of appropriate statistical technique.

OBSERVATIONS: Out of 100 patients with acute haemorrhagic stroke 92 patients had intracerebral haemorrhage and 8 patients had subarachnoid haemorrhage. (Table 1/Figure 1).

Among 100 cases of haemorrhagic stroke headache at onset was present in 70% of the patients, vomiting was present in 68% of patients, loss of consciousness was present in 84% of patients, hemiparesis was present in 82% of patients, seizure was present in 38% of patients, sensory loss was present in 7% of patients and aphasia was present in 52% of patients. (Table 2/Figure 2).

Out of 100 patients of acute haemorrhagic stroke 64% of patients had serum creatinine concentration more than 98umol/L. (Table 3/Figure 3).

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Out of 100 patients of acute haemorrhagic stroke at the time of presentation 74 patients (74%) had blood urea concentration more than 6.8mmol/L. (Table 4/Figure 4).

Patients were divided into two groups on the basis of eGFR. Group A (eGFR>60 ml/min/1.73 m² BSA) comprised of 71% of total stroke patients and group B (eGFR <60 ml/min/1.73 m² of BSA) consisted of 29% of total stroke patients.

In group A 7.05% of patients belonged to age group 18-40 years; 25.35% belonged to age group 40-65 years; 67.60% were of >65 years. In group B 3.45% of patients belonged to age group 18-40 years; 31.03% belonged to age group 40-65 years; 65.52% were of >65 years. (Table 6/Figure 6). In group A 63.38% of patients were males and 36.62% were females. In group B 62.07% of patients were male and 37.93% were females. (Table 7/Figure 7).

65.52% of patients in group B were obese (BMI>30kg/m²) while 50.71% of patients in group A were obese. (Table 8/Figure 8).

Among risk factors hypertension was seen in 61.97% of patients in group A compared to 68.96% of patients in group B. Diabetes mellitus was seen in 45.07% of patients in group A compared to 51.72% of patients in group B. Dyslipidemia was seen in 30.98% of patients in group A compared to 31.03% of patients in group B. Smoking was present in 47.89% of patients in group A compared to 48.27% of patients in group B. Alcoholism as a risk factor was present in 39.44% of patients in group A compared to 44.83% of patients in group B. History of Cardiovascular disease was present in 42.25% of patients in group A compared to 68.96% of patients in group B. Previous history of stroke/TIA was present in 21.13% of patients in group A compared to 27.56% of patients in group B. (Table 9/Figure 9).

Glasgow coma scoring of patients in both groups were done. (Table 10/Figure 10).

Out of 71 patients in group A, 14 (19.71%) patients died within 30 days of presentation and out of 29 patients in group B, 8 (27.58%) patients died within 30 days. (Table 11/Figure 11)

Out of 22 patients who died within 30 days of presentation 14 (63.60%) had serum creatinine >98umol/L. (Table 12/Figure 12).

Out of 22 patients who died within 30 days of presentation 15 (68.18%) had blood urea >6.8mmol/L. (Table 13/Figure 13).

DISCUSSION: To study renal function tests in patients with acute haemorrhagic stroke and to find association of abnormal renal function test in terms of adverse outcome, 100 cases of acute haemorrhagic stroke were evaluated.

Types of Stroke: Present study found that among 100 cases of haemorrhagic stroke, Intra-cerebral Haemorrhage accounted for 92% and subarachnoid haemorrhage for 8%.

However, similar study done by J Bamford et al (JNNP-1990; 53; 16-22).⁷ found incidence of Intracerebral haemorrhage to be 66% and Subarachnoid Haemorrhage to be 33%.

O G Nilsson et al (JNNP-2000; 69: 601-607),⁸ in their study (Incidence of Intracranial and subarachnoid Haemorrhage) found incidence of Intracranial Haemorrhage in 73.20% of cases and Subarachnoid Haemorrhage in 22.7% of cases. (Table 14).

eGFR: In this study 71% of patients (71 patients) of acute haemorrhagic stroke had eGFR>60ml/min/1.73m² of BSA (body surface area) and 29% of patients (29 patients) had eGFR<60ml/min/1.73m² of BSA. The results are comparable to study done by George Tsagalis et al

(2008),⁹ on study of renal dysfunction in stroke patients. They found that 28.08% Of Acute Stroke patients had eGFR<60ml/min/1.73m² of BSA. In study done by Hao Z et al (2010),¹⁰ they found out of 1758 stroke patients, 463 (26.3%) had eGFR<60ml/min/1.73m² of BSA. Naganuma M et al (2011),¹¹ in their study found that, out of 578 stroke patients Renal dysfunction was present in 32.20%. Their criteria for renal dysfunction was eGFR<60ml/min/1.73m² of BSA. Diange Liu et al (2012),¹² in their study to investigate the prevalence of decline in renal function in patients admitted for acute stroke, found that 45.10% of haemorrhagic stroke patients had eGFR<60ml/min/1.73m² of BSA (Table 15)

Serum Creatinine Concentration: In present study, out of 100 cases of acute haemorrhagic stroke, serum creatinine concentration > 98umol/L was seen in 64% of cases which was significant (P<. 001). The result was in contrast to similar study done by Ronald S Mc Walter et al⁵. In their study they found that serum creatinine > 98umol/L was seen in 36% of cases.

Blood Urea Concentration: 74 cases out of 100 cases (74%) had blood urea level > 6.8mmol/L which was significant (P<. 001). The result was comparable to study done by Ronald S Mc Walter et al.⁵ In their study they found that 60% of cases had blood urea level > 6.8mmol/L.

Outcome (All-cause Mortality within 30 days of Presentation) in Relation to Serum Creatinine Concentration and Blood Urea Concentration: Present study showed that out of 100 cases of acute haemorrhagic stroke, 22 cases died within 30 days of presentation. Of those 22 deaths, 14 cases belonged to group A (eGFR>60ml/min/1.73m²) and 8 cases belonged to group B (eGFR<60ml/min/1.73m²). Result was comparable to Study done by George Tsagalis et al.⁹

In the present study, out of 22 patients who died within 30 days of presentation, 14 patients (63.60%) had serum creatinine concentration >98umol/L (P<. 01). The result was comparable to study done by Ronald S Mc Walter et al.⁵ study, where they observed serum creatinine concentration >98umol/L in 59.52% of patients who died within 30 days of presentation. 15 deaths (68.10%) out of total 22 patients who died within 30 days of presentation, had blood urea level > 6.8mmol/L (P<.001). The result was comparable to similar study done by Ronald S Mc Walter et al.⁵ They found similar outcome in 66.85% of cases.

CONCLUSION: This study clearly indicated that renal dysfunction as evidenced by (a) eGFR <60 ml/min/1.73 m² of BSA, b) Sr creatinine >98umol/L & c) Blood urea >6.8mmol/L, are not only an important risk factor for acute haemorrhagic stroke but are also an independent predictor of mortality within 30 days of presentation.

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Type of stroke	No. of patients (%)
Intracerebral haemorrhage	92 (92%)
Subarachnoid haemorrhage	08 (8%)
Total	100 (100%)

Table 1: Distribution of patients according to type of haemorrhagic stroke

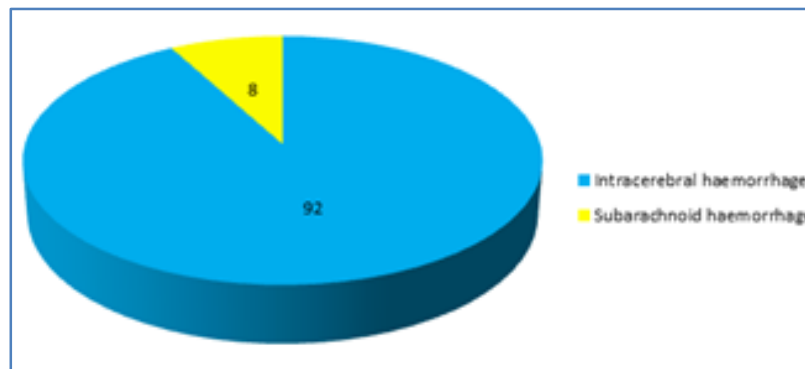


Fig. 1: Distribution of patients according to type of haemorrhagic stroke

Clinical Presentation	No. of patients (%)
Headache	70 (70%)
Vomiting	68 (68%)
Loss of consciousness	84 (84%)
Hemiparesis	82 (82%)
Seizure	38 (38%)
Sensory Loss	7 (7%)
Aphasia	52 (52%)

Table 2: Clinical presentation

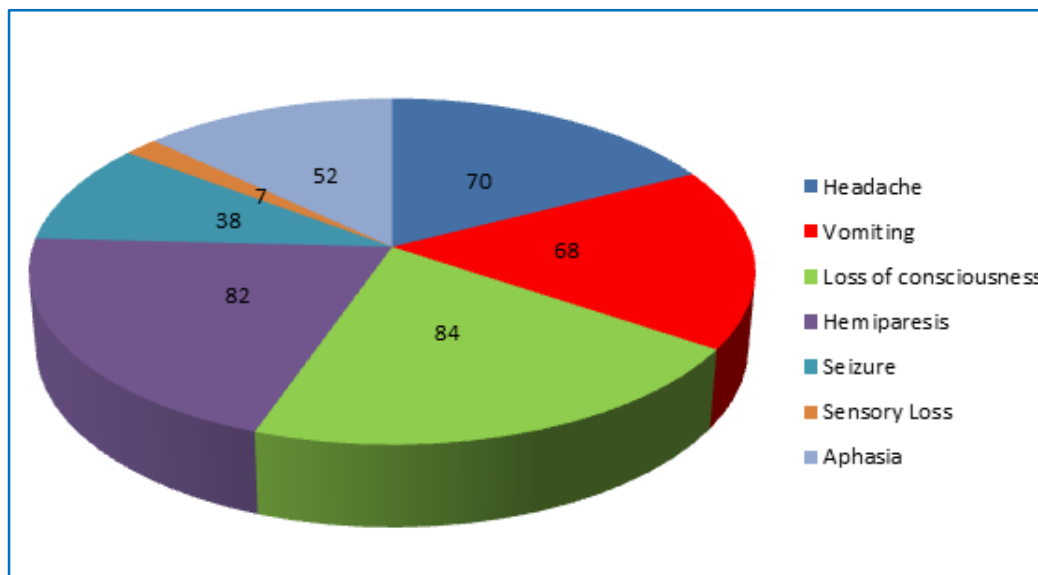


Fig. 2: Clinical presentation

Serum Creatinine(umol/L)	Cases of Acute Haemorrhagic Stroke
30-81	12(12%)
82-97	24 (24%)
98-118	31(31%)
>119	33(33%)

Table 3: Distribution of Patients according to Serum Creatinine concentration at time of presentation

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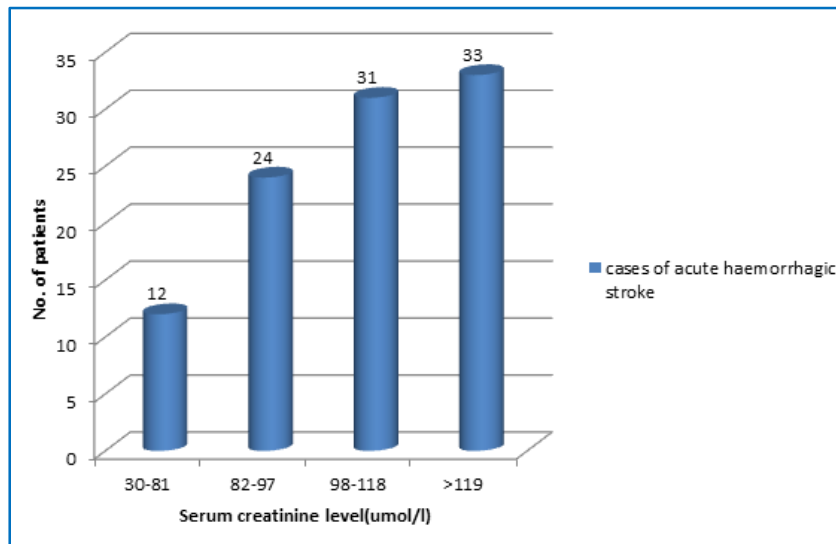


Fig. 3: Distribution of Patients according to Serum Creatinine concentration at time of presentation

Blood Urea (mmol/L)	Cases of Acute Haemorrhagic Stroke
1.8-5.2	8(8%)
5.3-6.7	18(18%)
6.8-8.9	32(32%)
>9	42(42%)

Table 4: Distribution of Patients according to Blood Urea concentration at time of presentation

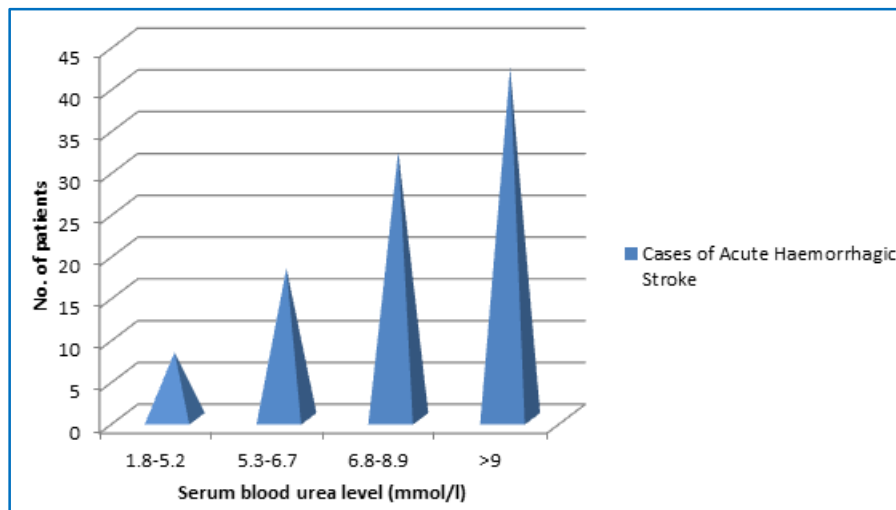


Fig. 4: Distribution of Patients according to Blood Urea concentration at time of presentation

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Group A (eGFR>60 ml/min/1.73 m ²)	71 (71%)
Group B (eGFR<60 ml/min/1.73 m ²)	29 (29%)
Total	100 (100%)

Table 5: Distribution of patients according to eGFR

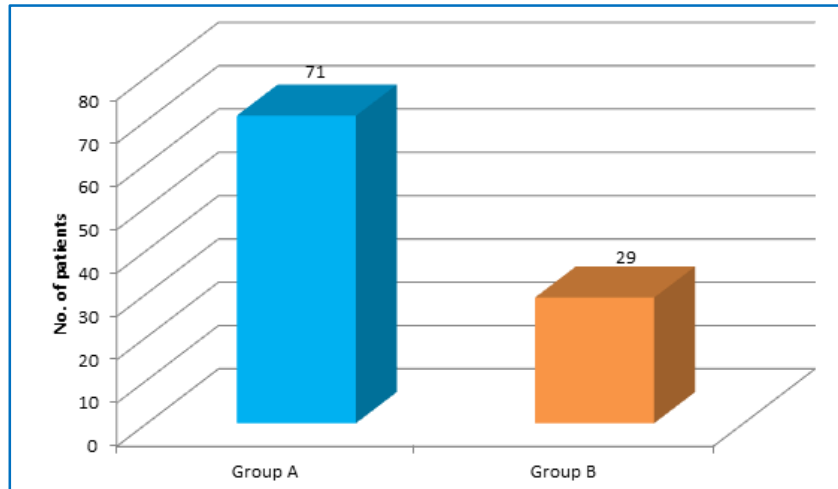


Fig. 5: Distribution of patients according to eGFR

Age (in yrs)	Group A	Group B
18-40	05 (07.05%)	01 (03.45%)
40-65	18 (25.35%)	09 (31.03%)
>65	48 (67.60%)	19 (65.52%)
Total	71 (100%)	29 (100%)

Table 6: Age distribution of the study group

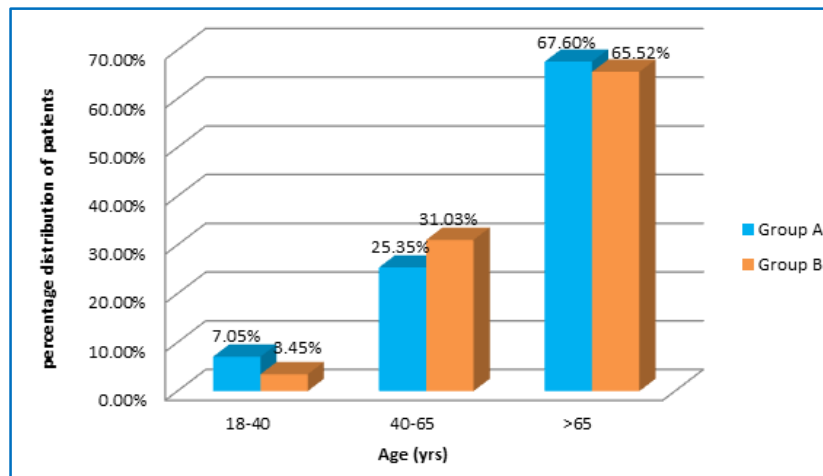


Fig. 6: Age distribution of the study group

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Sex	Group A	Group B
Male	45 (63.38%)	18 (62.07%)
Female	26 (36.62%)	11 (37.93%)
Total	71 (100%)	29 (100%)

Table 7: Distribution of patients on the basis of sex

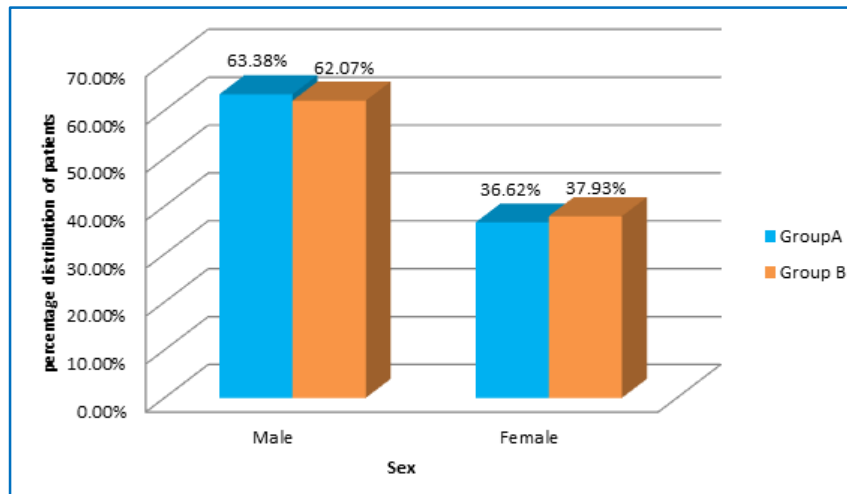


Fig. 7: Distribution of patients on the basis of sex

BMI (kg/ m ²)	Group A	Group B
<30	35 (49.29%)	10 (34.48)
>30	36 (50.71%)	19 (65.52%)
Total	71 (100%)	29 (100%)

Table 8: Distribution of patients according to BMI

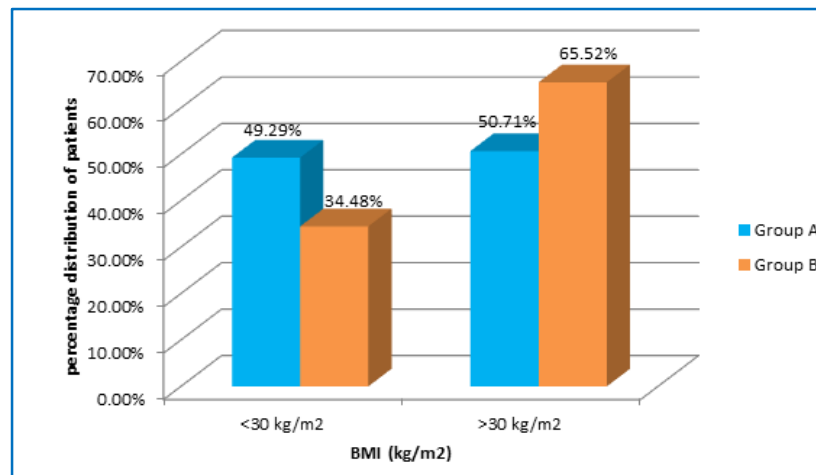


Fig. 8: Distribution of patients according to BMI

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Risk Factors	Group A	Group B
Hypertension	44 (61.97%)	20 (68.96%)
Diabetes Mellitus	32 (45.07%)	15 (51.72%)
Dyslipidemia	22 (30.98%)	9 (31.03%)
Smoking	34 (47.89%)	14 (48.27%)
Alcohol	28 (39.44%)	13 (44.83%)
Cardiovascular disease	30 (42.25%)	20 (68.96%)
Previous history of stroke/TIA	15 (21.13%)	8 (27.56%)

Table 9: Distribution of risk factors in both groups

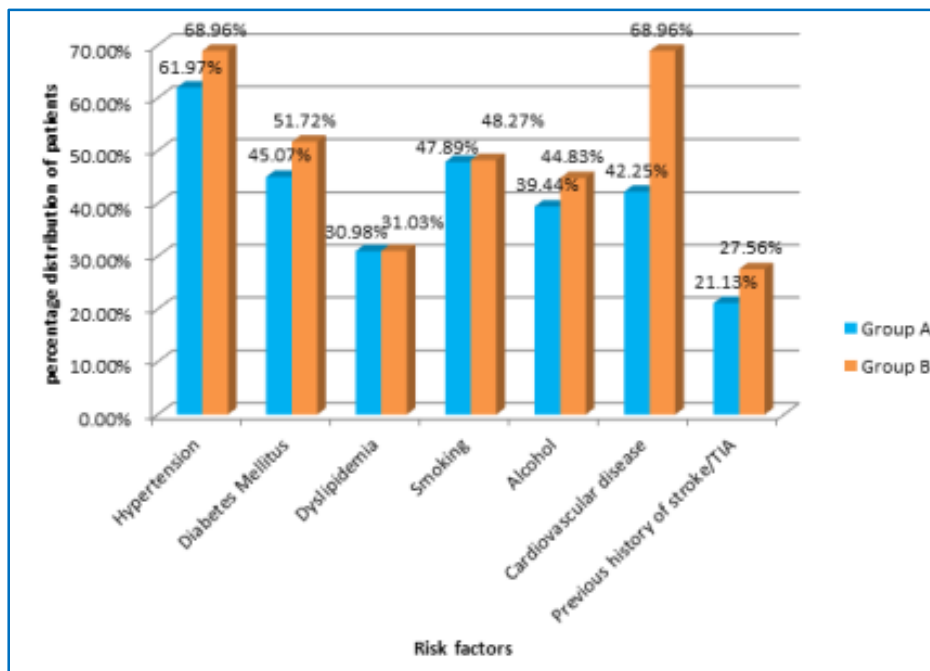


Fig. 9: Distribution of risk factors in both groups

GCS	Group A	Group B
3-4	08 (11.27%)	06 (20.68%)
5-8	26 (36.62%)	05 (17.34%)
9-13	27 (38.03%)	10 (34.48%)
>13	10 (14.08%)	08 (27.50%)
Total	71 (100%)	29 (100%)

Table 10: Glasgow Coma Scoring

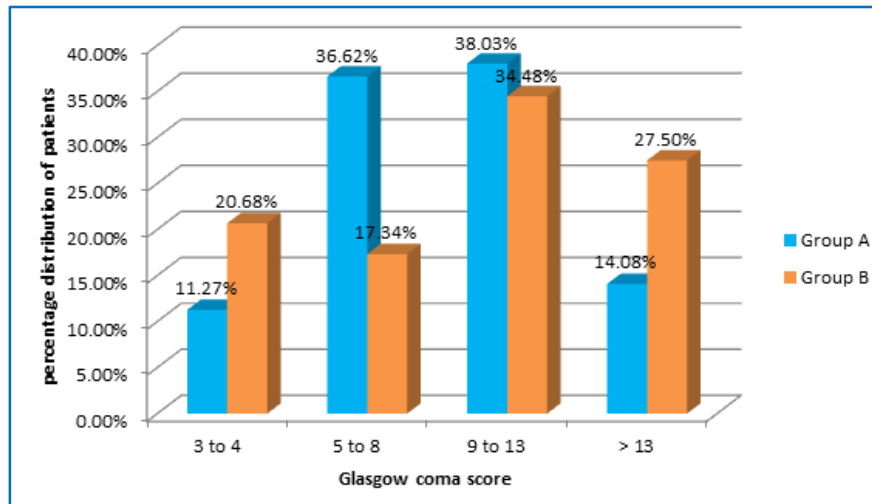


Fig. 10: Glasgow Coma Scoring

	Mortality	Total no. of patients
Group A	14(19.72%)	71
Group B	8(27.58%)	29

Table 11: Outcome (Overall Mortality within 30 days of presentation)

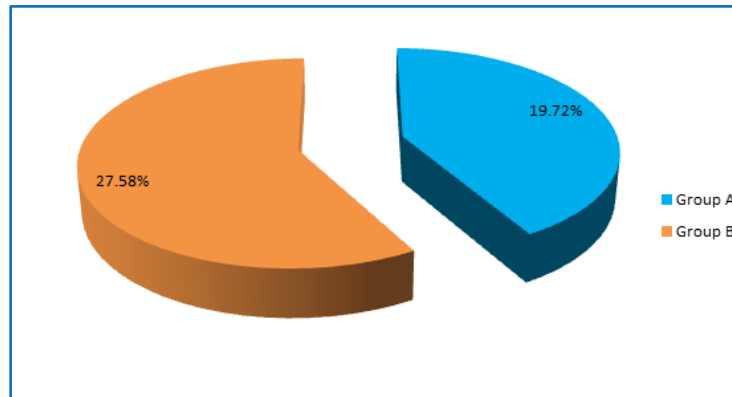


Fig. 11: Outcome (Overall Mortality Within 30 days of presentation)

Serum Creatinine(umol/L)	Outcome (Mortality within 30 days)
30-81	3(13.65%)
82-97	5 (22.75%)
98-118	6(27.25%)
>119	8(36.35%)

Table 12: Distribution of Overall Outcome (Mortality within 30 days) according to Serum Creatinine Concentration

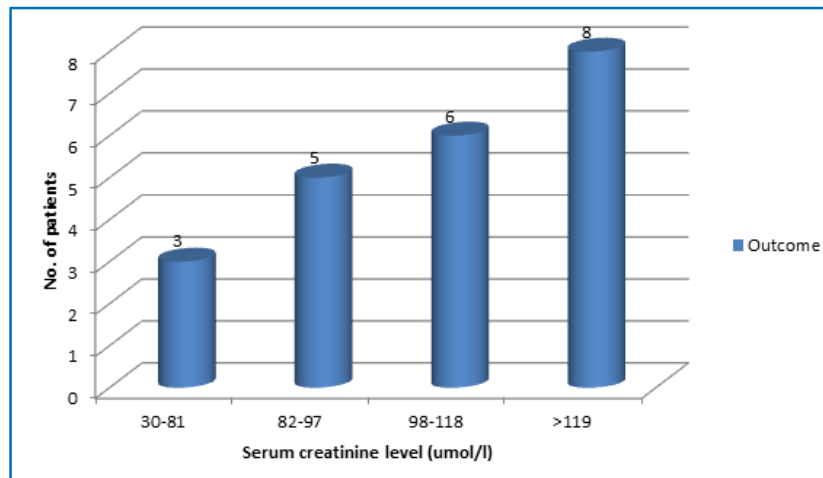


Fig. 12: Distribution of Overall Outcome (Mortality within 30 days) according to Serum Creatinine Concentration

Blood Urea(mmol/L)	Outcome (Mortality within 30 days)
1.8-5.2	2(9.15%)
5.3-6.7	5(22.75%)
6.8-8.9	7(31.75%)
>9	8(36.35%)

Table 13: Distribution of Overall Outcome (Mortality within 30 days) according to Blood Urea Concentration

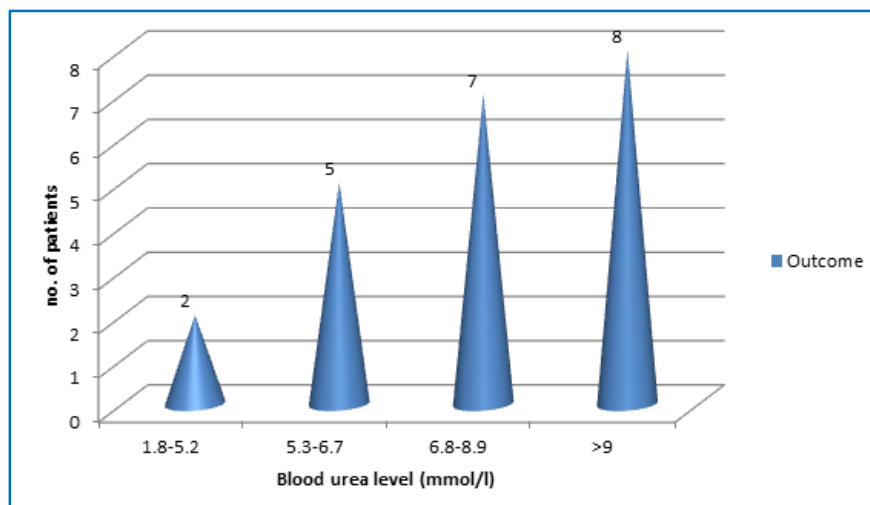


Fig. 13: Distribution of Overall Outcome (Mortality within 30 days) according to Blood Urea Concentration

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Types	Present Study	J Bamford et al ⁷	O G Nilsson et al, ⁸
Intracerebral haemorrhage	92%	66%	73.2%
Subarachnoid haemorrhage	8%	33%	22.7%

Table 14: comparison of type of stroke in different studies

Study	Renal Dysfunction
Present Study	29%
Tsagalis et al. ⁹	28.08%
Hao Z et al. ¹⁰	26.30%
Naganuma et al. ¹¹	32.20%
Diange Liu et al. ¹²	45.10%

Table 15: Comparison of Renal dysfunction among stroke patients in different studies on the basis of eGFR

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