PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS WITH STROKE: A PROSPECTIVE OBSERVATIONAL STUDY

THESIS

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AIIMS, JODHPUR **DR KASINA VENKATA AKHIL**

DECLARATION

I hereby declare that the thesis titled **"Predictors of outcome in critically ill patients with stroke: a prospective observational study"** embodies the original work carried out by me at All India Institute of Medical Sciences, Jodhpur.

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CERTIFICATE

This is to certify that the thesis titled "**predictors of outcome in critically ill patients with stroke: a prospective observational study**" is the bonafide work of Dr. KASINA VENKATA AKHIL carried out under our guidance and supervision, in the Department of Anaesthesiology and Critical Care, All India Institute of Medical Sciences, Jodhpur.

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"*Keep your face always towards the sunshine and the shadows will fall behind you.*"

(*Walt Whitman)*

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Dr Kasina Venkata Akhil

Dedicated to my

Patients,

Teachers, Family

&

My Friends…

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LIST OF ABBREVIATIONS

Abbreviation	Full Form
CVA	Cerebrovascular accident
ICU	Intensive care unit
NIHSS	National institute of health stroke scale
APACHE	Acute physiology and chronic health evaluation
CI	Confidence interval
GCS	Glasgow coma score
AIS	Acute ischemic stroke
ICH	Intracranial hemorrhage
SAH	Sub arachnoid hemorrhage
ED	Emergency department
BMI	Body mass index
ISC	Ischaemic stroke
WBC	White blood cells
TIA	Transient ischemic stroke
MI	Myocardial ischaemia
CAD	Coronary artery disease
HR	Heart rate
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
MAP	Mean arterial blood pressure
SpO2	Pulse oximeter saturation of arterial oxygen
CBC	Complete blood count
KFT	Kidney function test
LFT	Liver function test
TFT	Thyroid function test
PT	Prothrombin time
HbA1C	Glycosylated haemoglobin
Hs-CRP	High sensitivity c reactive protein
IL-6	Interleukin -6
ROC	Receiver operator characteristic
IQR	Interquartile range
CM	Centimetre
KG	Kilogram
M	Meter
HTN	Hypertension
DM	Diabetes mellitus
IHD	Ischemic heart disease
CKD	Chronic kidney disease
BPM	Beat per minute
MMHG	Millimetre mercury

°F	Degree in Fahrenheit
RR	Respiratory rate
Hb	Haemoglobin
NLR	Neutrophil lymphocyte ratio
PLR	Platelet lymphocyte ratio
Cr	Creatinine
Alb	Albumin
Glob	Globulin
Tot Bili	Total bilirubin
D bili	Direct bilirubin
TP	Total protein
SGOT	Serum glutamate oxaloacetic transaminase
SGPT	Serum glutamate pyruvate transaminase
ALP	Alkaline phosphatase
IU/L	International units per liter
APTT	Activated partial thromboplastin time
HDL	High density lipoprotein
LDL	Low density lipoprotein
Ch	Cholesterol
TG	Triglyceride
T3	Triiodothyronine
T4	Tetraiodothyronine
TSH	Thyroid stimulating hormone
MG	Milligram
DL	Deciliter
PG	Picogram
NG	Nanogram
MIU/L	Milli International units per liter
ML	Milliliter
DL	Deciliter
UG	Microgram
MMOL	Millimole
UMOL	Micromole
MEQ	Milli equivalent
L	Liter
IM	Inflammatory markers
AC	Anticoagulants
E	Electrolytes
RRT	Renal replacement therapy

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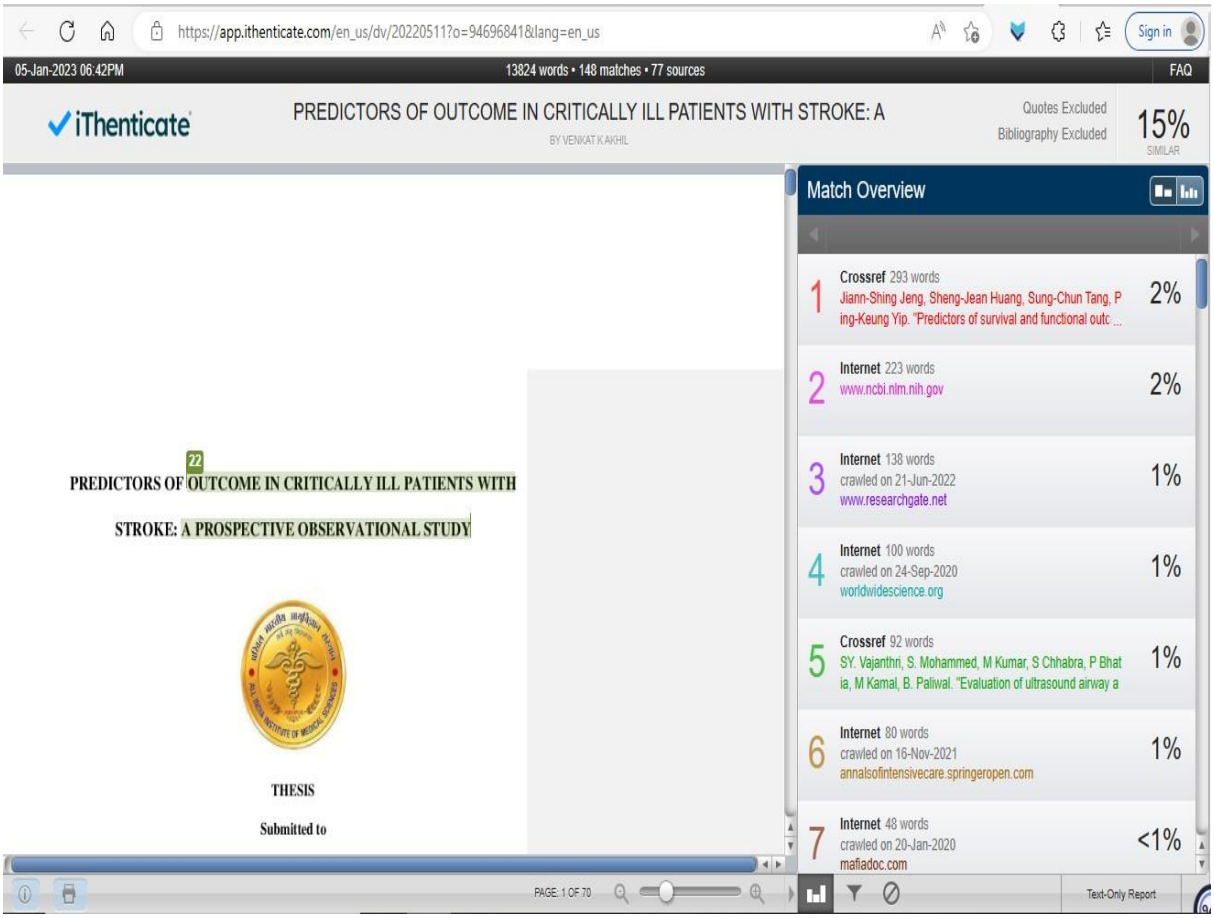
PLAGIARISM CHECK CERTIFICATE



SUMMARY

Background: Stroke is the leading cause of mortality and long-term disability world-wide. The accurate way to predict the likely long-term outcome (prognosis) for individual patients would help clinicians manage their patients and help relatives and patients come to terms with their changed circumstances. The present study aimed to find out the potential factors that can predict outcome of the critically ill stroke patients using the easily available data like demographics, comorbidities, clinical presentation and blood investigations (routine plus inflammatory marker) along with the other scores.

Material and Methods: We enrolled a total of 124 patients of either sex, aged above 18 years, diagnosed with ischemic or hemorrhagic stroke and admitted to ICU. The data recorded for each patient included demographic data, comorbidities, drug history, vitals, scores like GCS, NIHSS, APACHE II, routine investigations (CBC, KFT, LFT, TFT, PT, Lipid profile, HbA1C, Serum electrolytes), inflammatory markers, anticoagulation profile (protein C, protein S, antithrombin III), complications and therapies. The primary objective was to find an association between these data and in-hospital mortality. Secondary objectives included association between these data and mortality at 3-month and to find out the functional impairment at 3-months.

Results: Total 124 patients were included in final analysis; out of them 47 patients were diagnosed with hemorrhagic stroke and the remaining 77 with acute ischemic stroke. In the univariate analysis previous history of TIA/stroke; use of anti-hypertensive; hemorrhagic type of stroke; higher NIHSS and APACHE II (both at admission and at 24 hours); higher WBC count, NLR, PLR, blood urea, serum creatinine, serum lactate, and serum ferritin; lower GCS, serum T4, protein S, and antithrombin III; and requirement of vasoactive drug infusion, mechanical ventilation and renal replacement therapy were significantly different between survivors and non-survivors (p-value <0.05). Among these, APACHE II at 24 hours [OR (95% CI) 1.34 (1.07 to 1.7); p value= 0.01], need for vasoactive drug infusion [OR (95% CI) 1.63 (0.71 to 3.75); p-value= 0.024] and requirement of mechanical ventilation [OR (95% CI) 14.63 (1.78 to 115.5); p-value= 0.012] were found to be independent predictor of in-hospital mortality. These were also independent predictor [Odds raio (95% CI) 1.79 (1.22 to 2.64), p=0.003; 2.47 (1.04 to 5.87), p= 0.01 and 11.1 (1.67 to 74.2), p= 0.039 respectively] of 90-

day mortality. Around one third (19 out of 58) of the patients had good functional outcome (mRS 0-2) at 90-days after hospital discharge.

Conclusion: In critically ill stroke patients APACHE II score at 24 hrs, vasoactive drug infusion and requirement of mechanical ventilation during ICU stay are independent predictors of in-hospital and 90-day mortality.

INTRODUCTION

Cerebro-vascular accident (CVA) or stroke is the leading cause of mortality and long-term disability world-wide. It is the second leading cause of death and one of the commonest causes of disability in adults.[1] It is defined as sudden loss of brain function resulting from cerebral vascular disease. In 2016, stroke along with ischemic heart disease accounted for 15.2 million deaths worldwide. These diseases have remained the leading causes of death globally in the last 15 years. Many people with stroke are left with permanent disabilities. Although improvement in general intensive care unit (ICU) care, development of stroke units and effective reperfusion strategies in acute ischemic stroke accounted for the decreased mortality and disability-adjusted life-years in the last 20 years, but the burden of stroke is likely to remain high.[2–4]

The accurate way to predict the likely long-term outcome (prognosis) for individual patients would help clinicians manage their patients and help relatives and patients come to terms with their changed circumstances. Clinicians can get some idea of their patients' likely outcomes by assessing simple clinical variables. Previous studies have examined predictors of functional outcome or mortality after stroke and developed several predictive models.[5,6,6–11] Age, initial stroke severity, hyperglycemia or diabetes mellitus and stroke types constitute significant independent predictors of functional outcome and survival. Other predictors include gender, previous stroke, blood pressure, hyperthermia, and the volume of infarction or hemorrhage. Most of these studies have been done in stroke ward and enrolled patients with consecutive stroke or ischemic stroke patients, and some in hemorrhagic stroke. There have been a few studies done in ICU-admitted stroke patients.[12–15] Initial stroke severity, measured by National Institute of Health Stroke Scale (NIHSS), dependence on a ventilator, age, acute physiology and chronic health evaluation III (APACHE III) and diagnosis predicts in-hospital and 3-month mortality and poor outcome while age, APACHE III, and Glasgow Coma Score (GCS) predicts 1-year mortality. In addition, old age, previous stroke, and total anterior circulatory infarct were associated with poor outcome in ischemic stroke patients; old age, low body mass index and the presence of intraventricular hemorrhage were associated with poor outcomes in intracerebral hemorrhage patients.[12,13] The predictors of functional outcome at 1-year are admission APACHE III and hospital discharge Barthel Index scores.[13]

We hypothesized that the mortality (in-hospital and at 3-months) and functional status (at 3-months) of the critically ill stroke patients can be predicted using clinical, demographics,

laboratory and commonly used scoring (GCS, NIHSS, APACHE II, Barthel index etc.) system. The present study aimed to find out the potential factors that can predict outcome of the critically ill stroke patients by measuring the demographics, comorbidities, clinical presentation and blood investigations (routine plus inflammatory marker) along with the other scores.

AIMS AND OBJECTIVES

AIM: To find out association between various easily available patient data and outcome of critically ill stroke patients.

PRIMARY OBJECTIVE: To find out association between patient characteristics, clinical features, GCS, NIHSS, APACHE II, and laboratory data on the day of admission to ICU and in hospital mortality among critically ill stroke patients.

SECONDARY OBJECTIVE:

To find out the association between patient characteristics, clinical features, GCS, NIHSS, APACHE II, and laboratory data on the day of admission to ICU and 3-month mortality among critically ill stroke patients.

To find out the functional impairment at 3-months among critically ill stroke patients.

To devise a predictive model for prediction of in-hospital and 90-days mortality among critically ill stroke patients.

REVIEW OF LITERATURE

Stroke is a common event and a major cause of hospitalization, disability, and mortality worldwide.[14] Major therapeutic advances during the past decade, including development of dedicated stroke units, introduction of reperfusion therapy and interventional neuroradiology, and performance of acute neurosurgical interventions in selected patients have been shown to decrease mortality and improve disability-free survival.[16] However, a growing number of stroke patients require ICU admission for either neurological monitoring or the management of stroke complications, with 10–30% becoming critically ill.[17] In addition, stroke patients without treatment options are increasingly being admitted to the ICU to facilitate organ donation. Among patients with stroke, significant differences exist between those admitted to ICUs and those admitted to neurological wards or stroke units. The ICU group is characterized by greater neurological severity, moderate-to-severe consciousness impairment, need for mechanical ventilation, and high hospital mortality. Moreover, experts recently emphasized the importance of focusing research not only on short-term survival but also on long-term functional outcomes of critically ill stroke patients, in order to improve communication with patients and relatives and to determine the appropriate level of care.

Sauson Soldozy et al. (2022)[18] in order to anticipate long-term outcomes conducted a systematic review of articles from the years 1986 to 2018 from the Medline and pubmed database. The Biomarkers that are used to forecast a patient's long-term prognosis are made into broad categories inflammatory, peptide/enzymatic, oxidative/metabolic, hormone/steroid, and haematologic/vascular biomarkers. Scales such as the MRS, GCS, NIHSS, Barthel index, MMSE, and Beck Depression Inventory are used to classify the outcome. Statistical analysis did by the cochran Q test to assess p-heterogeneity. out of 183 articles 30 met criteria for meta-analysis. Five most common bio markers C-reactive protein (CRP; OR, 2.6; 95% CI, 1.6-.4; P=0.000), albumin (OR, 15.6; 95% CI, 3.2-75.9; P=0.00), copeptin (OR, 7.8; 95% CI, 1.7-34.7; P=0.01), D-dimer (OR, 6.6; 95% CI, 1.9-23.4; P=0.00) were all statistically predictive of functional outcome. The interpretation of the findings is restricted by limitations of the study biomarker connected with the research associated with the stroke itself or the confounding factor as well as different study designs, cohorts, methods of biomarker measures, outcome evaluations, and inconsistent analysis. Because there is a significant link with a biomarker that is more likely to be reported, considerable bias was found in the included research.

Thibut Carval et al (2022)[19] did a retrospective study in ICU admitted patients after acute stroke to describe clinical features and outcomes of the patient along with predicting good 6 month neurological outcome with mRS score in french university. A total 323 patients were admitted in the time period between 2014 to 2018 collected all data from electronic health records on day of admission, hospital discharge and on days of 28 and 180 after ICU admission. In his study the median age group was 67 (54.5-77), most common comorbidity was hypertension 155 (48%) followed by CAD and dyslipidemia. The most common stroke was hemorrhagic 248 patients, median GCS score 6 (4-10), SAPS II score 54 (35-64). Out of 323 patients 190 (58.8%) died in ICU, died in hospital was 198 (61.3) and died before 6 months 202 (64.5%). In this study factors associated with the good outcome (mRS<2) in univariate analysis after 6 months of ICU admission were age, GCS score, haemorrhagic stroke, persistent pupillary light reflex, and mechanical ventilation. In multivariate logistic regression analysis only age and GCS score were an independent factor associated with outcome [OR (95% CI) 0.93 (0.89-0.96) and 1.23 (1.07-1.40) respectively]. Major strength of study was larger sample size, and management of acute stroke remained unchanged during this study period while the limitation was single center recruitment and did not include sub arachnoid haemorrhage patients

Dmitriy Viderman et al (2020)[20] did a retrospective study in order to identify risk factors for medium to long term mortality among stroke patients who were hospitalised in a neuro critical care unit. Out of 148 patients included in this study, 84 were ischemic and 64 were haemorrhagic stroke patients. In these patients the most common comorbidities were hypertension, chronic heart failure and atrial fibrillation, median duration ICU stay was 7 days (1-68 days) (range) and in hospital mortality was 55 (37%). Among these patients, haemorrhagic stroke and ischemic stroke were 39% and 37% respectively. Respiratory failure is the most common complication developed by the 93 (63%) patients. Univariable analysis significant variables were used in multi variable analysis and male sex [HR (95% CI) 0.48 (0.22–0.98) and haemorrhagic stroke vs. ischemic stroke [HR (95%CI) 0.44 (0.23–1.22)] trended toward a lower risk of in-hospital mortality. Cerebral edema was associated with a higher risk of mortality [HR (95%CI) 2.45 (1.04–6.13)].

Fabio Pilato et al (2020)[21] did a single center prospective observational study in ICU on 158 patients who were admitted to neuro ICU after stroke with in 7 days who had LVO (large vessel obstruction) and received with IVT (intravenous thrombolysis) or IAMT (intra arterial mechanical thrombectomy). They compared the difference between good outcome (with

mRS <2) and poor outcome (with mRS>=3) at 3 months and at 6 months independently for demographic factors, comorbidities, scores, length of stay and different investigations. At 3 months, in multivariate logistic regression analysis (with the exception of the length of mechanical ventilation due to multicollinearity) and the results showed that IVT [OR (95% CI) 2.87 (1.05–7.83); p=0.039] and NGT-removal [OR (95% CI) 2.96 (1.07–8.13); p=0.035] were associated with good outcomes, whereas a high baseline NIHSS score [OR (95% CI) 0.80 for each point of increase (0.72–0.90); p < 0.001] was a predictor of poor outcomes after IAMT. At 90 days in multivariate logistic regression analysis showed that older age [OR (95% CI) 0.95 for each year of increase (0.92–0.99); p=0.020), hemorrhagic transformation [OR (95% CI) 0.31 (0.11–0.84); p=0.022), increased baseline NIHSS score [OR (95% CI) 0.81 for each point of increase (0.74–0.90); p<0.001) were predictors of poor outcomes after IAMT, whereas a mTICI score of 2b/3 was a predictor of good outcomes [OR (95% CI) 7.86 (1.65–37.39); p=0.010).

de Montmollin E et al[22] (2020) aimed to study the association of ICU admission factors, including the reason for intubation, with 1-year survival of acute stroke patients requiring mechanical ventilation. They conducted a secondary data use analysis of a prospective multicenter database (14 ICUs) between 1997 and 2016 on consecutive ICU stroke patients requiring mechanical ventilation at admission. Patients with stroke of traumatic origin, subdural hematoma or cerebral venous thrombosis were excluded. The primary outcome was survival at 1-year after ICU admission. Factors associated with the primary outcome were identified using a multivariable Cox model stratified on inclusion center. They identified 419 patients (age 68 [58–76] years, males 60%) with a Glasgow coma score (GCS) of 4 [3–8] at admission. Stroke subtypes were acute ischemic stroke (AIS, 46%), intracranial hemorrhage (ICH, 42%) and subarachnoid hemorrhage (SAH, 12%). At 1 year, 96 (23%) patients were alive. Factors independently associated with decreased 1-year survival were ICH and SAH stroke subtypes, a lower GCS score at admission, a higher non-neurological SOFA score. Conversely, patients receiving acute-phase therapy had improved 1-year survival. Intubation for acute respiratory failure or coma was associated with comparable survival hazard ratios, whereas intubation for seizure was not associated with a worse prognosis than for elective procedure. Survival did not improve over the study period, but patients included in the most recent period had more comorbidities and presented higher severity scores at admission. They conclude that in acute stroke patients requiring mechanical ventilation, the reason for intubation and the opportunity to receive acute-phase stroke therapy were independently

associated with 1-year survival. These variables could assist in the decision process regarding the initiation of mechanical ventilation in acute stroke patients.

Aurora Semerano et al (2020)[23] did a study on leukocyte counts and ratios comparing the predictive outcome of stroke patients independently of infection along with parenchymal hemorrhagic transformation. This observational retrospective study was carried out in Milan, Italy, on 510 stroke patients who were admitted within 4.5 hours and had no prior infections. At three months, the outcome was evaluated by mRS in the population that had survived, coupled with mortality and haemorrhagic transformation. For univariate and continuous variables statistical analysis using the Mann-Whitney test and the Pearson Chi Square test was performed. For each outcome variable, performed a multivariate regression analysis. It is confirmed that better functional outcome with low NL-R, higher Lymphocyte count and higher eosinophil count. Death within 3 months associated with High NL-R and low eosinophil counts. NL-R showed the highest predictive values for good functional outcome and mortality at 3 months (respectively 0.740 and 0.843 as area under the curve, AUC). Both neutrophil counts and NL-R had good predictive values for the development of parenchymal haemorrhage (respectively 0.756 and 0.747 AUC). Interestingly, the interaction term between NL-R and poststroke infections resulted significant (p = 0.016), with a stronger relationship between NL-R and 3-month outcome in patients without infections, compared to those with post-stroke infections (OR [95%CI] = 0.733 [0.659–0.816] and 0.940 [0.792–1.115], respectively). The total dependability of frequently automated counts is the study's only limitation. Its strengths include assessments of all leukocyte subsets after stroke and precise inclusion criteria to analyse the relationships by reducing confounding factors.

Xiao-Guang Zhang et al (2020)[24] did a retrospective study in china between 2016 to 2018 to find out association between various inflammatory risk markers and ischemic stroke outcome and subtype. In this study they included 3013 patients and etiology of stroke subtypes were classified as a trial of org in acute stroke treatment (TOAST). Age (years) of patient mean (SD) 73 (13), mean SBP, CRP, WBC, neutrophil, lymphocyte and IL-6 was 147 (20.5), 18.5 (37.1), 7.42 (2.72), 68.0 (12.3), 25.0 (10.2), and 52.8 (228) respectively. Most common comorbidity was hypertension (72%) followed by diabetes (57%) and AF (atrial fibrillation) (9.6%). The mean NIHSS score was 4.65 (6.07). According to TOAST classification, 175 (6.69%) were CE (cardiac embolism) subtype, 1,364 (52.14%) were LAA (large artery occlusion) subtype and 1,077 were (41.17%) SAO (small artery occlusion) subtype. WBC, neutrophil count, IL-6 and CRP were significantly higher in CE or LAA supporting the role

of chronic inflammatory mechanisms in stroke. A Naive Bayesian classifier was used to estimate risk factors with the outcome of mortality, NIHSS, Barthel index and mRS. They found that neutrophil, lymphocyte and CRP have a higher prediction ability than TOAST subtypes for mortality prediction and for disability prediction with mRS count of neutrophil and lymphocyte best prediction. IL-6 and CRP were found as independent predictors only for mortality, stroke severity and mRS but not for Barthel index. Only neutrophil lymphocyte ratio was found as independent predictor along with neutrophil count for all of these 4 outcomes.

Perrine Bouvet et al (2019)[25] did a retrospective study on long term functional outcome of adult stroke patients who were admitted in intensive care unit and requiring mechanical ventilation. A total of 274 stroke patients who needed mechanical ventilation within seven days of admission to the centre were studied for demographic information, comorbidities, specific treatments, SAPS II score, GCS, Logistic Organ Dysfunction scale, baseline performance status and need for mechanical ventilation. Utilising consultation summaries, one-year functional outcome and mortality outcome variables were assessed to determine any associations between independent and outcome variable by using logistic regression analysis. This study found three variables associated with mortality illness first one is severity at ICU admission as assessed with the SAPS II [OR (95% CI), 1.07 (1.05-1.10) per SAPS II point; p<0.001), anisocoria [OR (95% CI) 5.26 (1.76-15.80); p=0.003), and sepsis at ICU admission [OR (95% CI) 0.40 (0.19-0.85); p=0.02). Four variables were independently associated with poor neurologic outcome: SAPS II [OR (95% CI) 1.07 per point (.05-1.10)], acute respiratory failure at ICU admission [OR (95% CI) 19.28 (2.72-413)], and anisocoria at admission [OR (95% CI) 2.17 (0.94-5.40)] were associated with poor outcome, whereas sepsis at admission [OR (95% CI) 0.26 (0.11-0.57)] was protective against poor outcome. Limitations of the study is single centre design, retrospective whose progress made during last year's study may have influenced the long-term outcome.

Mariëlle K. van Valburg et al (2018)[26] did a retrospective observational study to predict long term all causes mortality and functional outcome of adult stroke patients admitted to ICU. They evaluated 131 critically ill stroke patients and collected data on age, gender, time of admission, APACHE II score, reason for ICU admission, data of CT angiography, different routine investigations and final outcome after 1 year. They found that best predicted long-term all-cause poststroke mortality contained high APACHE II score, impaired consciousness (GCS score ≤ 8) as reason for ICU admission, low GCS sum score after 24 hours and absence

of brainstem reflexes. For every point higher on the APACHE II score, mortality was increased by 11.9% [HR (95% CI) 1.12 (1.07–1.17)]. When impaired consciousness (GCS score ≤ 8) was the reason for admission, patients had a three-fold chance to die [HR (95% CI) 3.05 (1.08–8.66)]. When brainstem reflexes were absent at ICU admission, patients had a 2.35-fold chance to die as compared to patients in whom brainstem reflexes were present at ICU admission [HR (95% CI) 2.35 (1.02-5.40)]. For outcome after 1- year poor functional outcome with mRS (3-6) found that APACHE II score, chances for poor functional outcome increased by 21.5% [OR (95% CI) 1.21 (1.07–1.37)]. If mass effect was shown on CT scan, patients had a 8.55-fold chance to have a mRS score higher than 2 after 1 year compared with patients who did not have a mass effect on CT scan [OR (95% CI) 8.55 (1.01-71.43)]. Main limitation of this study was retrospective design, misclassification and missing data. Study did in modest sample size, single center with highly populated in Urban region patients limiting external validity.

Alexander F. Bautista et al[27] (2017) did a retrospective observational cohort study on early prediction of prognosis in elderly acute stroke patients, this model included stroke type (intracerebral hemorrhage vs ischemic stroke: odds ratio [95% CI] of 0.92 [0.50–1.68] and subarachnoid hemorrhage vs ischemic stroke: 1.0 [0.40–2.49]), year (1.01 [0.66– 1.53]), age (1.78 [1.20–2.65] per 10 yr), smoking (8.0 [2.4–26.7]), mean arterial pressure less than 60mm Hg (3.08 [1.67–5.67]), Glasgow Coma Scale (0.73 [0.66–0.80] per 1 point increment), WBC less than 11K (0.31 [0.16–0.60]), creatinine (1.76 [1.17–2.64] for 2 vs 1), congestive heart failure (2.49 [1.06–5.82]) and warfarin (2.29 [1.17–4.47]). In summary age, smoking, congestive heart failure, warfarin use, Glasgow Coma Scale, mean arterial pressure less than 60mm Hg, admission WBC, and creatinine levels independently associated with mortality. The model had internal area under the curve of 0.83 (0.79–0.89) after adjustment for over-fitting, indicating excellent discrimination and concluded that baseline medical problems, clinical severity, and basic laboratory tests available within the first 12 hours of admission provided strong independent predictors of in-hospital mortality in elderly acute stroke patients.

Angelika Alonso et al (2015)[28] did a retrospective study in ICU patients for prognosis of stroke. A total 347 patients were enrolled and underwent standard stroke workup including risk factors, NIHSS and RASS. They assessed outcome after rehabilitation with mRS scare (<=3 defined as a good outcome of the patient). Out of 347 patients, ischemic stroke were 252 (72%) and ICH were 95 (27.4%). The most common comorbidity was hypertension

(83%) followed by atrial fibrillation (40%). The most common reason for ICU implication was neurological complication (46%), cardiac (23%) and respiratory (12%). Total 143 patients were died in this ischemic and hemorrhagic were 64 and 79 respectively in this significant higher mortality in ICH with p-value <0.001 and further mortality was associated with old age and need for mechanical ventilation (p<0.001). Patients who developed neurological complications like recurrent stroke, secondary haemorrhage , brain edema and epilepsy are more likely associated with mortality (p<0.001). Median NIHSS score was 12 (5-18). Total 143 patients died in this ischemic and hemorrhagic stroke were 64 and 79 respectively. Median mRS after rehabilitation was 4, outcome after rehabilitation was associated with good outcome in younger patients (p<0.008) and longer stay during rehabilitation (p=0.022). The outcome was not different in ischemic and hemorrhagic stroke and patients who received thrombolysis and not (p-value 0.27 and 0.92) respectively. Finally, out of several factors, negative outcome factors were age, coma at admission, high NIHSS score, need for mechanical ventilation and haemorrhagic stroke.

Moon et al (2014)[29] did a study in ICU patients of stroke of both hemorrhagic and ischemic stroke patients mainly comparing APACHE II and SAPS II score in predicting the mortality along with the GCS and NIHSS. Total 542 patients included in study over 2 years with median age of 56 (7-88). Hemorrhagic stroke patients were 60.2% and ischemic stroke patients were 39.8%. The Mortality of hospital stay was 27% and 23.7% for both types of strokes respectively. The mean APACHE II, SAPS II, GCS and NIHSS scores calculated within 24 hours of admission to the ICU were 35.12±23.73%, 35.34 ± 24.48%, 9.43 ± 4.18 and 21.63± 12.14, respectively. They found all these 4 scores good in predicting mortality (p< 0.001). In this study they found that APACHE II and SAPS II score better in predicting mortality and severity of disease than GCS and NIHSS in calibration curves. ROC curve showed a slightly better prediction of mortality for APACHE II in hemorrhagic stroke patients and SAPS II in ischemic stroke patients. The GCS and NIHSS were inferior in predicting mortality in both patient groups.

Jiann-Shing Jeng et al[12] (2007) performed a study on predictors of survival and functional outcome in acute stroke patients admitted to the stroke intensive care unit. a total of 850 acute stroke patients were included in the analysis. Of these patients, 491 (57.8%) were male and 359 (42.2%) were female with a mean age of 65.3 ± 14.4 years. Five hundred and eight (59.8%) patients were diagnosed as having had an ischemic stroke, and 341 (40.2%) as having had a non-traumatic ICH. Five hundred and eleven (60.1%) patients arrived at ED

within 3 h after stroke onset. The average length of ICU stay was 9.4± 8.8 days and the total length of hospital stay (including rehabilitation) was 37.4±32.0 days. The mean and median initial NIHSS scores were 17.7±9.6 and 17 (10–24), respectively that indicated moderate to severe neurological deficit. Of all patients, 66 (7.8%) had received neurosurgery, 70 (8.2%) had tracheostomy, and 278 (32.7%) had mechanical ventilation. Seventy (13.8%) patients with ischemic stroke received thrombolytic therapy. Of the medical complications occurred in the acute stage, respiratory tract infection was noted in 426 (50.1%) patients; urinary tract infection, 251 (29.5%); respiratory failure, 233 (27.4%); upper gastrointestinal bleeding, 110 (12.9%); sepsis, 57 (6.7%); post-stroke seizure, 53 (6.2%); acute coronary syndrome, 17 (2%); and deep vein thrombosis, 8 (0.9%). Of all patients, 3 months after the onset of stroke, 140 (16.5%) were dead; 179 (21.1%), alive and cared for in institutional settings; and 531 (62.4%), were alive and living. Multivariate analysis showed increased risk of poor functional outcome of stroke patients at discharge included older patients, requiring ventilator aid, a higher NIHSS score, a lower BMI value, and the presence of intraventricular hemorrhage, total anterior circulatory infarct type.

Navarrete-Navarro P et al[13] (2003) did a multicentre, prospective, observational study in 28 Spanish hospitals with the aim to analyse 1-year mortality and functional disability outcomes and resource use in critical stroke patients admitted to ICU. They enrolled patients admitted for acute stroke and collected of data on severity by Apache III and GCS; neurological lesion, hospital and 1-year mortality; functional disability at 1 year by Barthel Index and Glasgow Outcome Scale; ICU length of stay, life support techniques, and neurosurgical interventions. They studied 132 patients [21% with subarachnoid haemorrhage (SAH), 58% intracerebral haemorrhage (ICH), 20% ischaemic stroke (ISC)] having mean APACHE III 63±29 and ICU stay 13±12 days. Seventy four percent of these required mechanical ventilation. Hospital and 1-year mortality was 33% (22%-ISC, 32%-SAH, 37%-ICH) and 53.8% (66%-ISC, 39%-SAH, 54%-ICH), respectively. Age, APACHE III, and diagnosis defined hospital mortality. Age, APACHE III, and Glasgow Coma Score defined 1-year mortality. Barthel Index score improved ($P<0.001$) between discharge and 1 year; 73% of patients presented severe disability at discharge vs. 26% at 1 year; 8% minimal/no disability at discharge vs. 43.3% at 1 year. Only 17% of SAH patients presented severe disability at 1 year. Admission Apache III and hospital discharge Barthel Index scores were related to functional outcome at 1 year. They conclude that critical stroke patients are characterized by high severity of illness, elevated resource consumption, and poor outcomes that are mainly influenced by severity and

age. Glasgow Coma Score-measured neurological severity is the main determinant of future functional capacity, which is greater at 1 year.

William whitely et al[30] performed a systematic review of the literature and meta-analysis of the association between IL-6 and poor outcome after stroke to place study in the context of previous research. They recruited 844 patients; mortality data were available in 844 (100%) and functional outcome in 750 (89%). After appropriate adjustment, the odds ratios for the association of markers and poor outcome (comparing the upper and the lower third) were IL-6 [OR (95% CI) 3.1 (1.9-5.0)]; C-reactive protein [OR (95% CI) 1.9 (1.2-3.1)]; fibrinogen [OR (95% CI) 1.5 (1.0-2.36)]; white cell count [OR (95% CI) 2.1 (1.3-3.4)]; and glucose [OR (95% CI) 1.3 (0.8-2.1)]. The results for IL-6 were similar to other studies. Raised levels of markers of the acute inflammatory response after stroke are associated with poor outcomes.

Marcio Francisco Lehmann et al[31] aimed to study to evaluate the association between inflammatory and metabolic markers and short time outcome with acute ischemic stroke subtypes. A total of 121 patients was classified according to TOAST criteria, such as large artery atherosclerosis (LAAS), lacunar infarct (LAC), cardioembolic infarct (CEI), other determined etiology (ODE), and undetermined etiology (UDE). The functional impairment was evaluated within the first eight hours of stroke and the outcome after three-month follow-up using the modified Rankin Scale. Blood samples were obtained up to 24 h of stroke. Compared with 96 controls, patients with LAAS, CEI, and LAC subtypes showed higher levels of white blood cells, high-sensitivity C-reactive protein (hsCRP), interleukin 6 (IL6), metalloproteinase 9 (MMP-9), glucose and platelets, insulin, insulin resistance, and homocysteine were higher in LAC, ferritin was higher in LAAS, and total cholesterol (TC) was lower in LAAS and CEI. When stroke subtypes were compared, insulin was higher in LAAS vs. LAC. The results underscored the important role of the inflammatory response and metabolic changes in the pathogenesis of ischemic stroke subtypes that might be considered on the initial evaluation of stroke patients to identify those that could benefit with individualized therapeutic strategies that taken into account these markers after acute ischemic event.

MATERIALS AND METHODS

Study Design

Prospective Observational Study

Study Setting

This study was carried out in the Adult Intensive Care Unit (AICU) under the Department of Anaesthesiology & Critical Care, AIIMS Jodhpur.

Study duration/Sample size

We enrolled patients admitted to AICU between March 2021 and August 2022.

Study Participants

- **Inclusion criteria:** Adult (>18 years) patients, presented with focal neurological deficit of vascular origin, diagnosed as stroke either haemorrhagic or ischaemic radiologically and requiring admission in ICU.
- **Exclusion criteria:**
    1. Patients with traumatic intracerebral haemorrhage or other types of brain injury
    2. Patient with anoxic–ischemic brain injury following cardiac arrest
    3. The patient/relatives who refused to give Informed consent

Methodology:

The present study was carried out in the department of Anaesthesiology and Critical Care at AIIMS, Jodhpur after getting approval from institutional ethics committee [Institutional Ethics Committee, All India Institute of Medical Sciences, Jodhpur 342005 (Raj.); Certificate Reference Number: AIIMS/IEC/2021/3329; dated 12/03/2021; approved by Dr Parveen Sharma] and informed written consent from patient‘s relatives. We registered the study prospectively at the clinical trial registry of India (CTRI: www.ctri.nic.in) [(Ref. No. CTRI/2021/04/033173, Date of Registration: 27/04/2021)].

The demographic, clinical, laboratory, imaging and outcome data of each admitted stroke patient were recorded. The record of each patient included age, gender, height, weight, body mass index (BMI), socioeconomic status, comorbidities (Hypertension (HTN)/ Diabetes (DM)/ asthma/ tuberculosis (TB)/ Dyslipidemia/ Atrial Fibrillation (AF)/ Previous Stroke or transient ischemic attack (TIA)/ Previous myocardial infarction (MI)/ coronary artery disease

(CAD)/ Illicit Drugs/ Obesity/ sleep apnea/ Chronic kidney disease (CKD)/ others), drug history, clinical manifestations, vitals [including heart rate (HR), systolic (SBP), diastolic (DBP), and mean arterial blood pressure (MAP) taken with the patient in the supine position, respiratory rate (RR), body temperature and pulse oximeter saturation of arterial oxygen (SpO2) at ICU admission]. Neurological status (determined by GCS and NIHSS), APACHE II score at the admission and at 24 hours, laboratory data (complete blood counts (CBC), kidney function test (KFT), liver function test (LFT), thyroid function test (TFT), prothrombin time (PT), lipid profile, haemoglobin A1C (HbA1C), high sensitivity C reactive protein (Hs-CRP), Procalcitonin (PCT), d-Dimer, Ferritin, interleukine-6 (IL-6), Protein C/ Protein S, Antithrombin, Homocysteine, Fibrinogen, Lactate and serum electrolytes for first 24 hours), complications and therapies (need for and time on mechanical ventilation; administration of hypotensive and vasoactive drug infusions or antiarrhythmic, sedative, and relaxant drug infusions; and use of ventricular catheter, intracranial pressure monitoring, angiographic/intravascular procedures, neurosurgery, and tracheostomy).

Stroke was defined using the World Health Organisation (WHO) definition and included ischemic stroke and non-traumatic intracranial hemorrhage (ICH).[19] According to the Bamford criteria, ischemic stroke was categorized as the total anterior circulation stroke, partial anterior circulation stroke, lacunar stroke, and posterior circulation stroke.[20] ICH was categorized as primary hypertensive, other secondary etiology, or undetermined etiology. The diagnosis of stroke and its subtypes was made based on the clinical features and the data collected by laboratory examinations, such as brain imaging [computed tomography (CT) or magnetic resonance image (MRI)], echocardiography, ultrasonography of extracranial and/or intracranial arteries, and angiography (MR or conventional angiography).

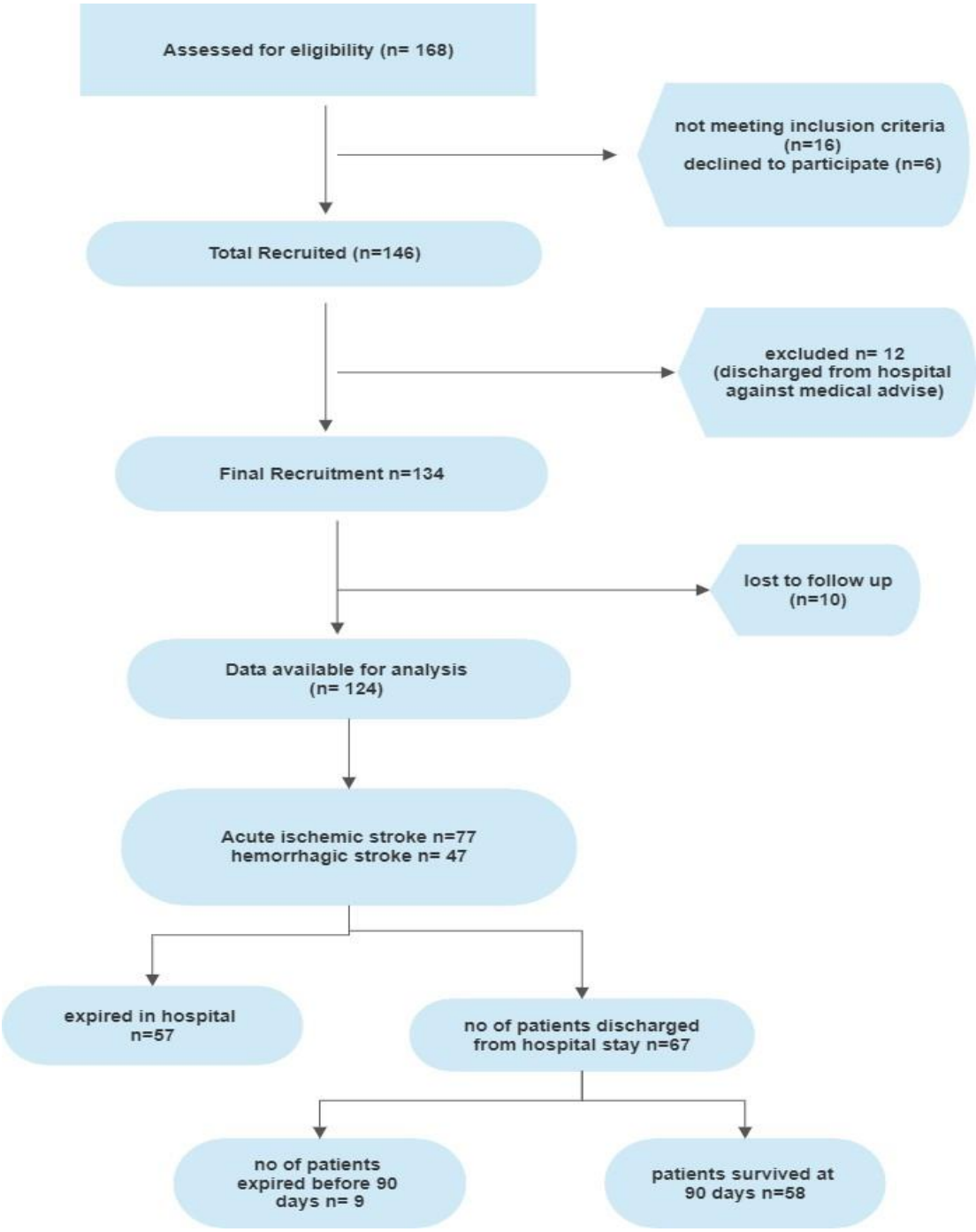
Patients' status was followed for at least 90-days and categorized as death, survival with institutional care and survival living at home. Functional outcomes at discharge assessed using the modified Rankin scale [21] and Barthel index.[22] A poor functional outcome was defined as a modified Rankin scale >2 or a Barthel index <80.

Statistical Analysis Plan

Data collected during the study was compiled using Microsoft Excel spreadsheets. Statistical analysis was carried out using SPSS version 23.0 (Statistical Package for Social Sciences, Inc., Chicago, IL). Normality of data was tested with Kolmogorov– Smirnov one-sample test. Data were presented as mean ± standard deviation (SD) for normally distributed quantitative variables and as median (IQR) (range) for ordinal variables and quantitative variables with

non-normal distribution. Categorical variables were presented as absolute numbers or percentages. Based on the outcome patients were categorised as survived and non-survived. The demographic, comorbidities, vitals at admission, neurological status (NIHSS and GCS), APACHE II score at the admission and at 24 hours, laboratory data (routine investigation and inflammatory markers), specific and non-specific treatment received in the ICU were compared between groups. Student‘s _t‘ test and $\chi 2$ test were used to analyse continuous and categorical data respectively. Quantitative variables with non-normal distribution and ordinal variables were analysed using Mann-Whitney test. P value <0.05 was considered as significant. The odds ratio and their 95% CI of the significant predictors of mortality after stroke onset was calculated. All univariate predictor variables with a p-value <0.05 were taken in the multivariate regression.

RESULTS



During the study period, a total 168 patients with stroke were admitted to the intensive care unit. Out of them, twenty-two patients were excluded for various reasons. Remaining one hundred and forty-six patients were recruited. Twelve patients left the hospital against medical advice before the outcome. The final recruitment included one hundred and thirty-four patients. Out of these ten patients lost to follow up finally data from one hundred and twenty-four patients included in data analysis. In those the total acute ischemic stroke patients were seventy-seven and haemorrhagic stroke patients were fourty seven.

Table 1: Distribution of study population as well as both groups according to different age groups and comparison of median age (years) between both groups

Age (years)	Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	Median Diff. (95% CI)	p-value
<40	16 (12.9)	9 (13.4)	7 (12.2)	-	0.99
41-60	49 (39.5)	26 (53)	23 (40.3)		
>60	59 (47.5)	32 (54.2)	27 (47.3)		
Median (IQR) (range)	60 (50, 70) (22-93)	60 (47, 69) (22-87)	60 (50, 72) (23-93)	0 (-7.1 to 4.0)	0.72

The above table displays the number and proportion of stroke cases under different age (years) groups in study population, survivors and non-survivors as well as comparison of median (IQR) age between survivors and non-survivors. Sixteen (12.9%) patients had age < 40 years, out of them 9 (13.4%) survived while 7 (12.2%) did not survive. Forty-nine (39.5%) patients were between 41-60 years, out of them 26 (53%) survived while 23 (40.3%) died. Fifty nine (47.5%) patients had age > 60 years, out of them 32 (54.2%) survived and 27 (47.3%) did not survive. There was no difference in the survival among all the age groups (p=0.99). The median (IQR) (range) age of the study population, survivors and non-survivors was 60 (50, 70) (22-93), 60 (47, 69) (22-87) and 60 (50, 72) (23-93) respectively. Mann Whitney U test was applied to compare median age between survivors and non-survivors which showed a median difference (95% CI) of 0 (-7.1 to 4.0) with p-value of 0.72 i.e., age of the patient did not affect survival of the critically ill stroke patients.

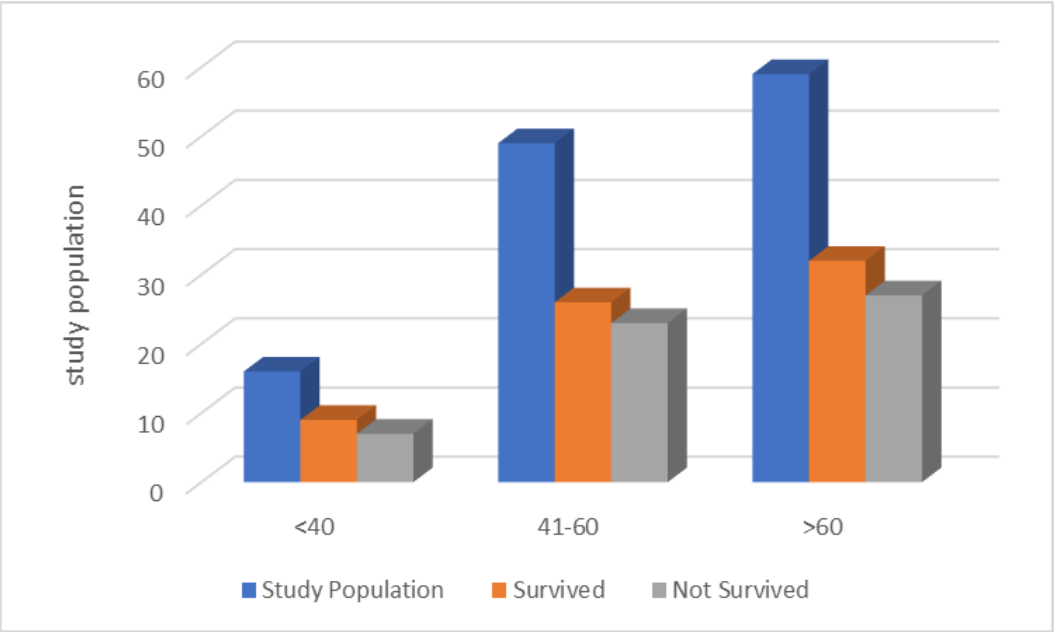


Figure 1: Number of patients with different age groups in study population, survivors and non-survivors.

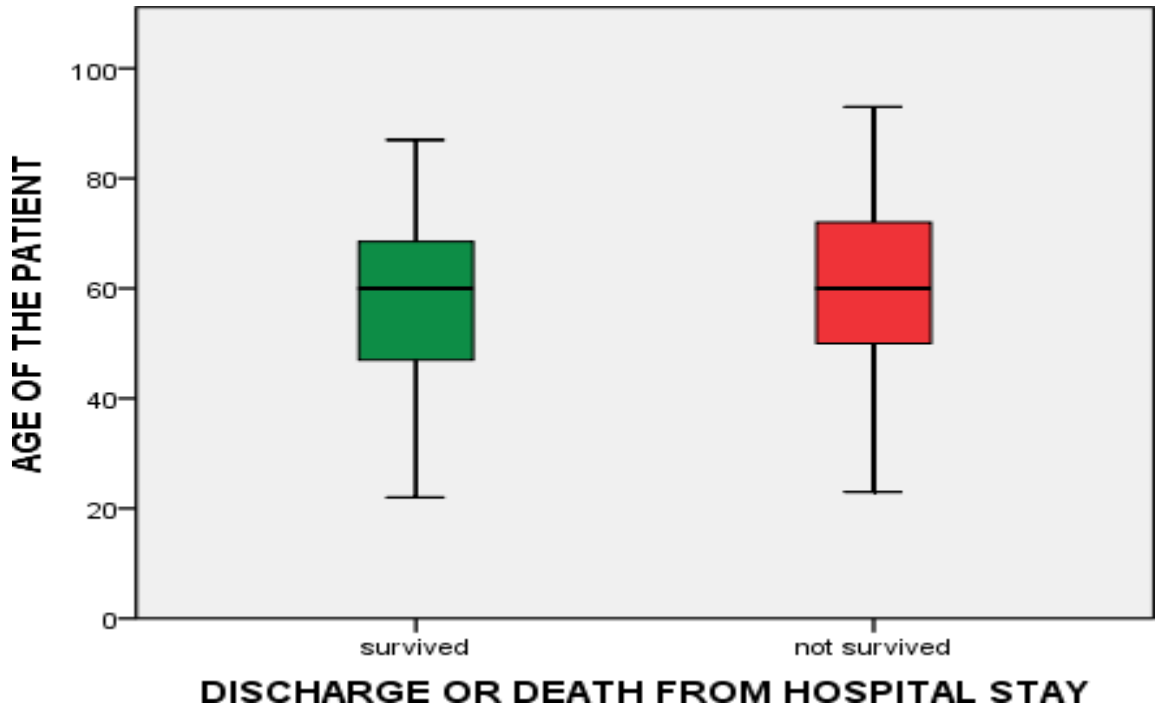


Figure 2: Box plot for comparison of median (IQR) (range) age between survivors and non-survivors.

Table 2: Distribution of study population as well as both groups according to gender and comparison of gender between both groups

Gender	Study Population (n = 124) (%)	Survived (n = 67) (%)	Not Survived (n = 57) (%)	χ^2; p-value
Female	31 (25%)	21 (67.74)	10 (32.25)	3.13; 0.08
Male	93 (75%)	46 (49.46)	47 (50.53)	

The above table displays the number and proportion of stroke cases according to gender in study population, survivors and non-survivors. Out of 124 patients, 31 (or 25%) were female and 93 (or 75%) were male. Among females, 21 (67.9%) survived while 10 (32.2%) died. Among males, 46 (49.4%) survived while and 47 (50.5%) died. The Chi square test was used to compare the survival between gender which showed a p value of 0.08, which was statistically insignificant i.e., gender of the patient did not affect survival of the critically ill stroke patients.

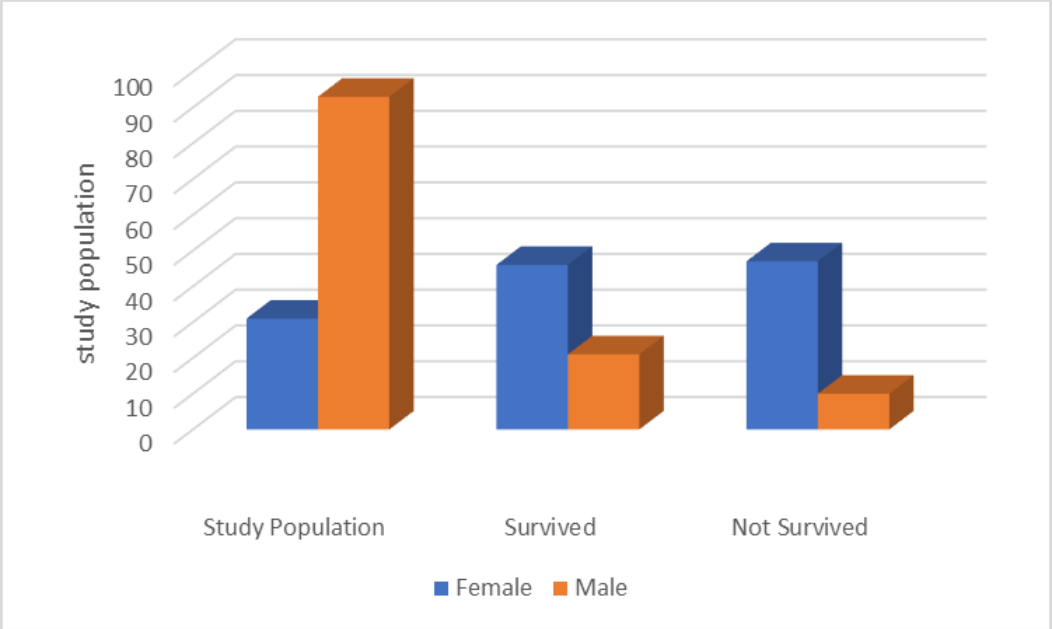


Figure 3: Number of patients with different gender in study population, survivors and non-survivors.

Table 3: Distribution of study population as well as both groups according to different height groups and comparison of median height between both groups

Height (cm)	Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	Median Diff (95% CI)	p-value
<150	2 (1.6)	2 (3)	-	-	-
150-170	94 (75.8)	49 (73.1)	45 (79)		
>170	28 (22.5)	16 (23.9)	12 (21)		
Median (IQR) (range)	164 (159, 163) (154-178)	168 (160, 170) (147-178)	166 (159, 169) (154-178)	2 (-1.98 to 2.6)	0.55

The distribution of the study population by height (cm) group is shown in the above table. Out of 124 patients, 2 (1.6%) were under 150 cm. In individuals whose height ranged from 150 to 170 cm were 94 (75.8%), out of them 49 (73.1%) survived and 45 (79%) died. Out of the 28 (22.5%) patients with a height of >170 cm, 16 (23.9%) survived, while 12 (21%) patients died. The median (IQR) (range) height of study population, survivors and non-survivors was 164 (159, 163) (154-178), 168 (160, 170) (147-178) and 166 (159, 169) (154-178) respectively. Mann Whitney U test was applied to compare median height between survivors and non-survivors which showed a median difference (95% CI) of 2 (-1.98 to 2.6) with p-value of 0.55 i.e., height of the patient did not affect survival of the critically ill stroke patients.

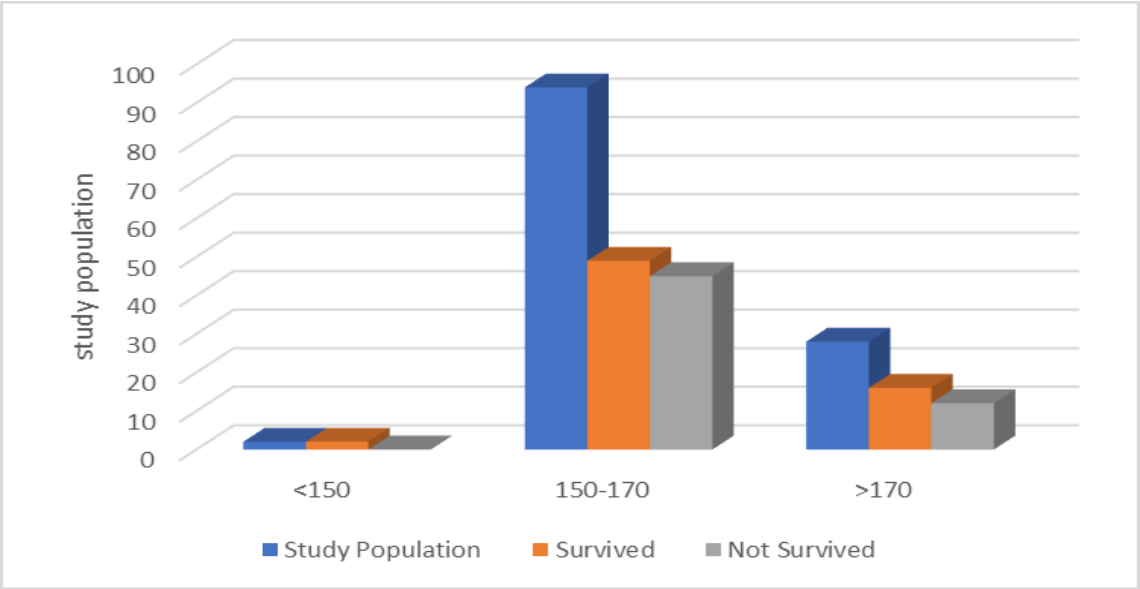


Figure 4: Number of patients with different height groups in study population, survivors and non-survivors.

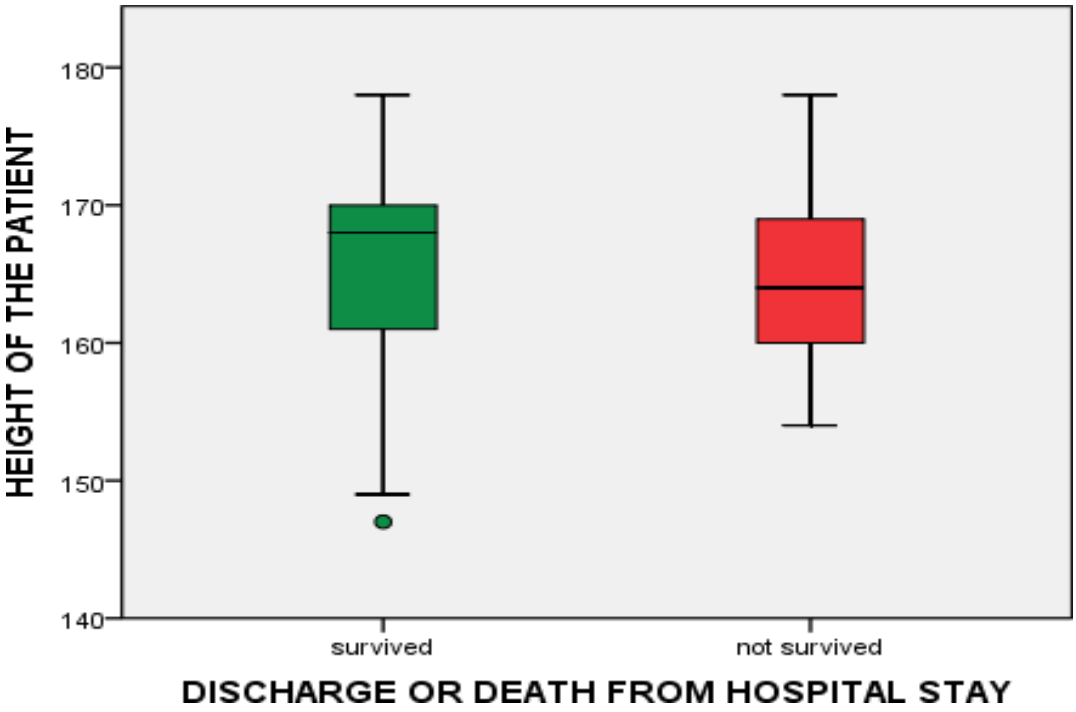


Figure 5: Box plot for comparison of median (IQR) (range) height between survivors and non-survivors.

Table 4: Distribution of study population as well as both groups according to different weight groups and comparison of median weight between both groups

Weight (kg)	Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	Median Diff (95% CI)	p-value
< 50	6 (4.8)	3 (4.4)	3 (5.2)	-	-
50-70	64 (51.6)	37 (55.2)	37 (65)		
> 70	54 (43.5)	26 (38.8)	28 (49.1)		
Median (IQR) (range)	68 (59.25, 78) (46-100)	68 (59, 79) (48-100)	69 (59, 79) (46-98)	1 (-4.9 to 4)	0.81

The above table shows the study population distribution according to the weight (kg) group. Patients with weight < 50 kg were 6 (4.8%), out of them 3 (4.4%) patients survived and 3 (5.2%) died. Patients with weight between 50-70 kg were 64 (51.6%), out of them 37 (55.2%) survived and 37 (65%) patients died. Patients having weight >70 kg were 54, out of them 26 (38.8) survived and 28 (49.1) died. The median (IQR) (range) weight of study population, survivors and non-survivors was 68 (59.25, 78) (46-100), 68 (59, 79) (48-100) and 69 (59, 79) (46-98) respectively. Mann Whitney U test was applied to compare median weight between survivors and non-survivors which showed a median difference (95% CI) of 1 (-4.9 to 4.0) with p-value of 0.81 i.e., weight of the patient did not affect survival of the critically ill stroke patients.

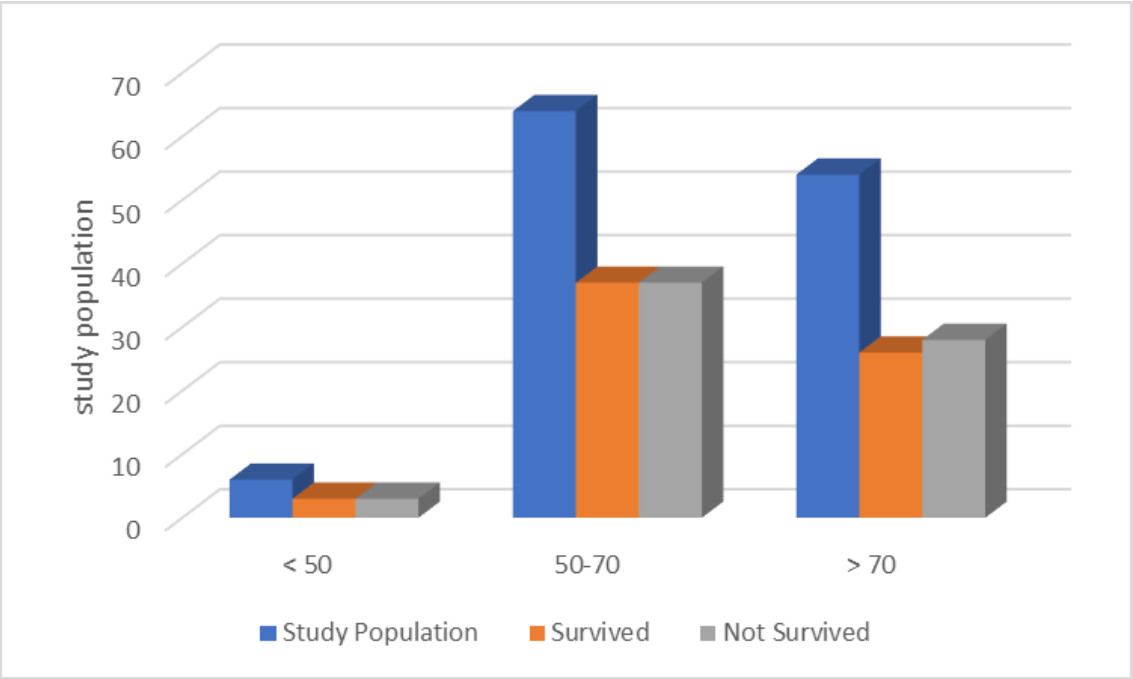


Figure 6: Number of patients with different weight groups in study population, survivors and non-survivors.

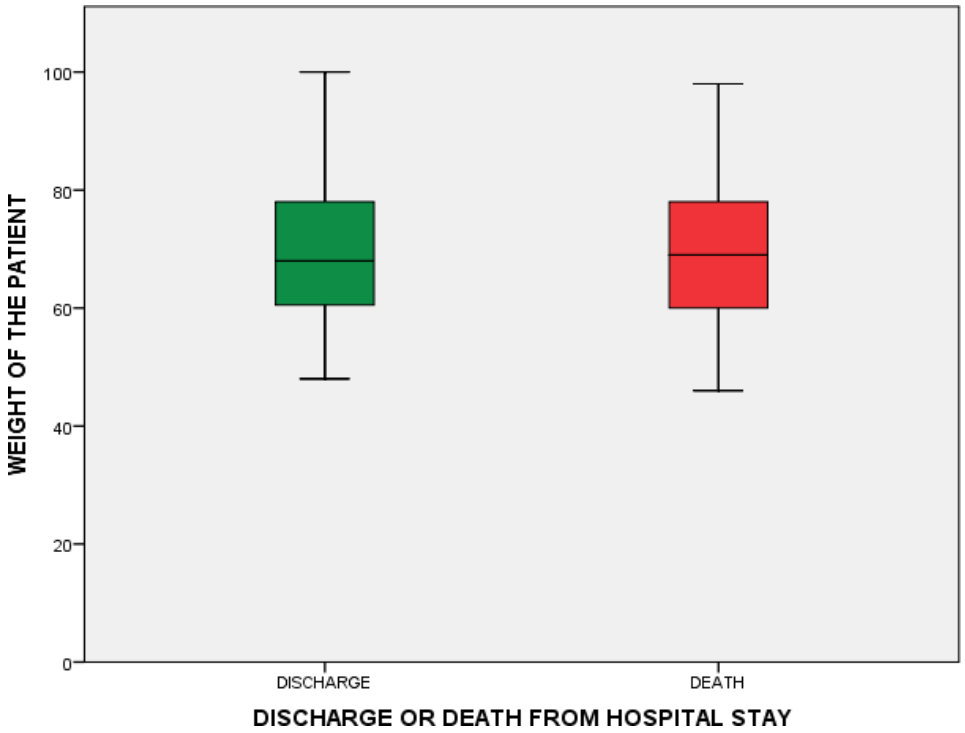


Figure 7: Box plot for comparison of median (IQR) (range) weight between survivors and non-survivors.

Table 5: Distribution of study population as well as both groups according to different BMI groups and comparison of median BMI between both groups

BMI (kg/m^2)	Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	Median Diff (95% CI)	p-value
< 18.5	2 (1.6)	1 (1.5)	1 (1.7)	-	-
18.6–24.9	58 (46.8)	33 (49.2)	25 (43.8)		
25.0-29.9	49 (39.5)	26 (38.8)	26 (45.6)		
>30.0	15 (12.1)	7 (10.4)	8 (14)		
Median (IQR) (range)	25.2 (22.3, 28.3) (18.2-36.4)	24.9 (22.5, 28.3) (17.2-35.4)	25.5 (22.1, 28.4) (18.2-36.4)	0.64 (-1.6 to 1.1)	0.91

The distribution of the study population according to different BMI (kg/m^2) categories is shown in the above table. Patients with BMI < 18.5 were 2 (1.6%), out of them one (1.5%) survived and one (1.7%) died. Patients with BMI 18.6 to 24.9 were 58 (46.8%), out of them 33 (49.2%) survived and 25 (43.8%) died. Patient with BMI between 25 to 29.9 were 15 (12.1%), out of them 7 (10.4%) survived and 8 (14%) died. Patients with BMI > 30 were 15 (12.1%), out of them 7 (10.4%) survived and 8 (14%) died. Median (IQR) (range) BMI of the study population, survivors and non-survivors was 25.2 (22.3, 28.3) (18.2-36.4), 24.9 (22.5, 28.3) (17.2-35.4) and 25.5 (22.1, 28.4) (18.2-36.4) respectively. Mann Whitney U test was applied to compare median BMI between survivors and non-survivors which showed a median difference (95% CI) of 0.64 (-1.6 to 1.1) with p-value of 0.91 i.e., BMI of the patient did not affect survival of the critically ill stroke patients.

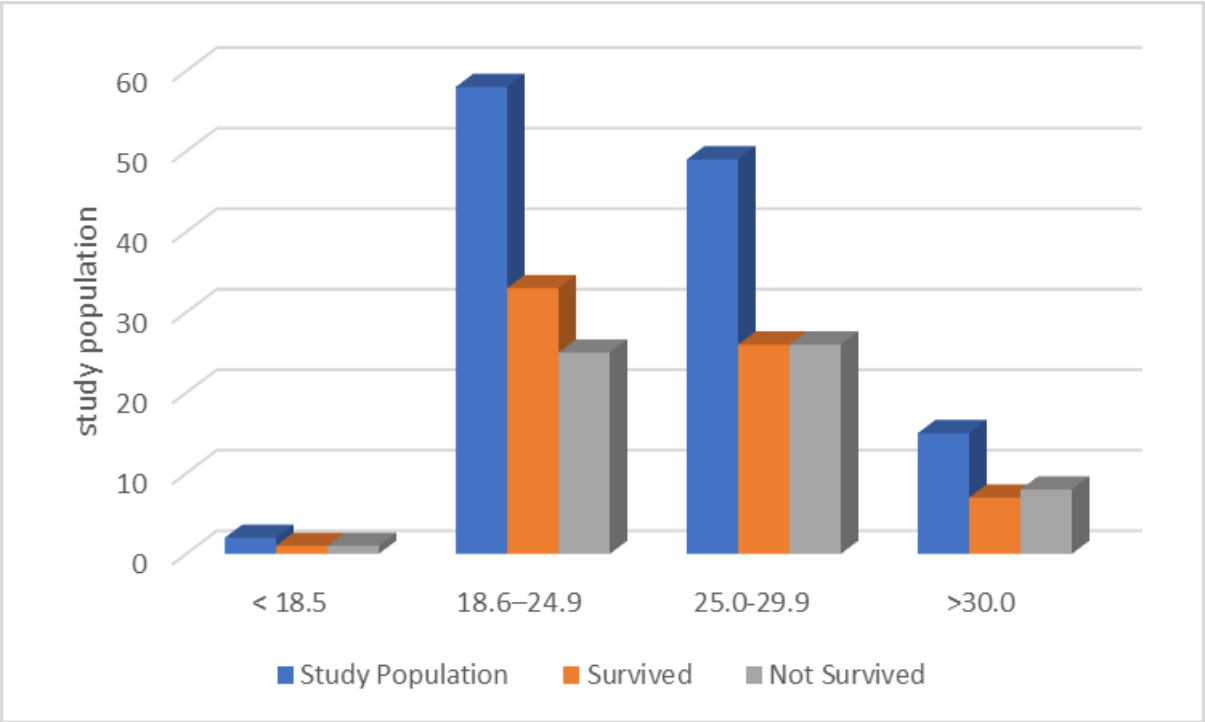


Figure 8: Number of patients with different BMI groups in study population, survivors and non-survivors.

Figure 9: Box plot for comparison of median (IQR) (range) BMI between survivors and non-survivors.

Table 6: Distribution of study population as well as both groups according to different socioeconomic groups and comparison of socioeconomic status between both groups

Socio economic status (Class)	Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	p-value
Lower	13 (10)	6 (9)	7 (12.2)	0.764
Lower Middle	38 (31)	19 (28.3)	19 (33.3)	
Upper Middle	47 (38)	28 (41.8)	21 (36.8)	
Upper	26 (21)	14 (21)	12 (21)	
Median (IQR) (Range)	3 (2, 3) (1-4)	3 (2, 3) (1-4)	3 (2, 3) (1-4)	0.48

The above table displays the number and proportion of stroke cases under different socioeconomic groups in study population, survivors and non-survivors as well as comparison of median (IQR) socioeconomic status between survivors and non-survivors. Among 124 patients, 13 (10%) patients were from a lower socioeconomic class, in those 6 (9%) patients survived and 7 (12.2%) died. Thirty eight (31%) patients belong to the lower middle class, out of which 19 (28.3%) survived and 19 (33.3%) died. Patients belonging to the upper middle class were 47 (38%) in those 28 (41.8%) survived and 21 (36.8%) died. There are 26 (21%) patients of the Upper class in those 14 (21%) discharged and 12 (21%) died. There was no difference in survival among all the socioeconomic classes (p=0.76). The median (IQR) (range) socioeconomic class of study population, survivors and non-survivors was 3 (2, 3) (1-4), 3 (2, 3) (1-4) and 3 (2, 3) (1-4) respectively. Mann Whitney U test was applied to compare median socioeconomic class between survivors and non-survivors which showed a p-value of 0.48 i.e., socioeconomic class of the patient did not affect survival of the critically ill stroke patients.

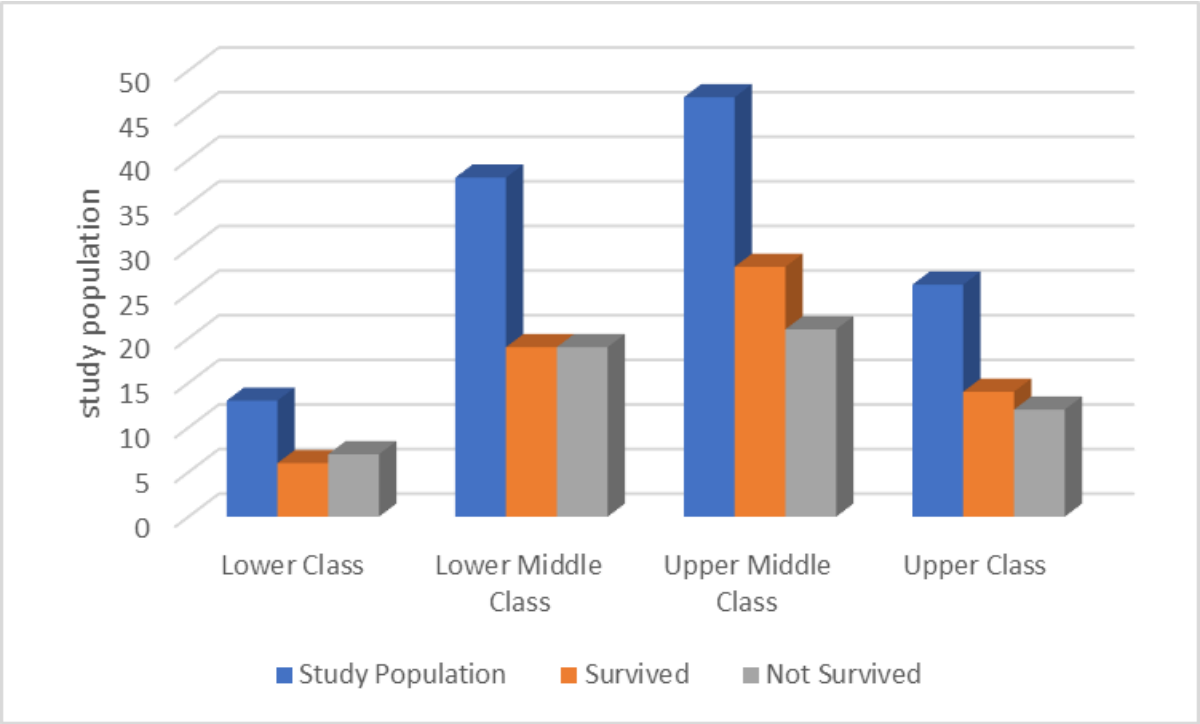


Figure 10: Number of patients with different socio-economic class groups in study population, survivors and non-survivors.

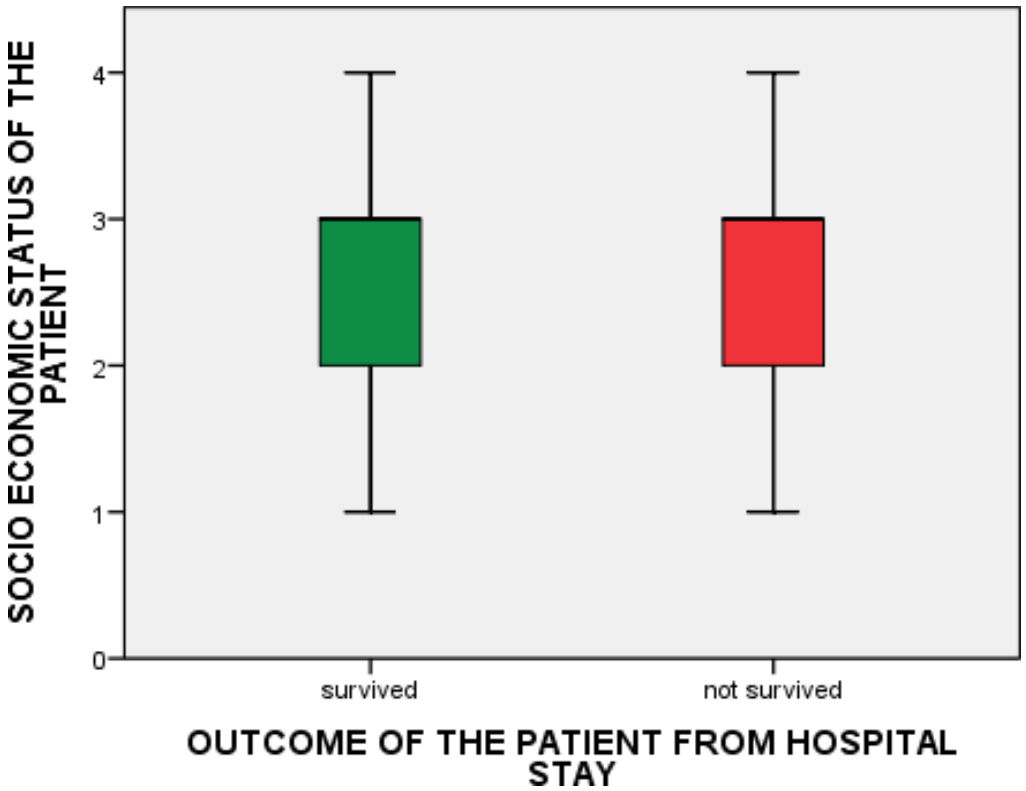


Figure 11: Box plot for comparison of median (IQR) (range) socio-economic class between survivors and non-survivors.

Table 7: Distribution of study population as well as both groups according to residential status and comparison of residential status between both groups

Residential status	Study Population (n = 124) (%)	Survived (n = 67) (%)	Not Survived (n = 57) (%)	p-value
Rural	78 (62.9)	43 (55.12)	35 (44.87)	0.10
Urban	46 (37.1)	24 (52.17)	22 (47.82)	

The above table displays the number and proportion of stroke cases under different residential status in study population, survivors and non-survivors. In the study population, patients belonging to rural areas were 78 (62.9%); in those 43 (55.12%) survived and 35 (44.87%) died. Forty six (37.1%) belonged to urban areas, among them 24 (52.17%) survived and 22 (47.82%) died. The Chi square test was used to compare the survival between residential status groups which showed a p value of 0.10, which was statistically insignificant i.e. residential status of the patient did not affect survival of the critically ill stroke patients.

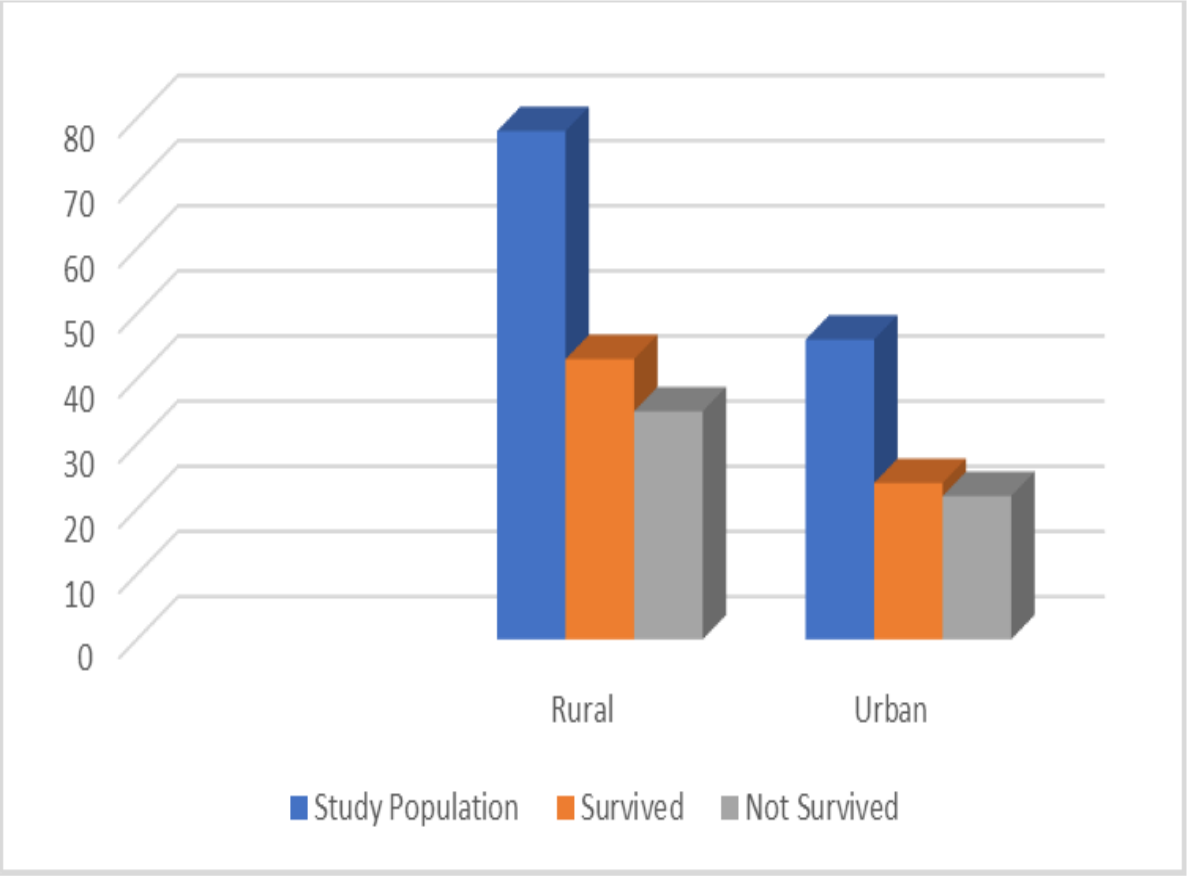


Figure 12: Number of patients with different residential status groups in study population, survivors and non-survivors.

Table 8: Distribution of study population as well as both groups according to the presence of co-morbidities and comparison of co-morbidities between both groups

Co-Morbidity	Study Population (n = 124) (%)	Survived (n = 67) (%)	Not Survived (n = 57) (%)	p-value
HTN	78 (62.9)	37 (47)	41 (52)	0.055
DM	38 (30.6)	18 (47)	20 (52)	0.322
IHD	21 (16.9)	11 (52)	10 (47)	0.868
H/O Previous stroke or TIA	22 (17.7)	7 (31)	15 (68)	**0.021**
CKD	12 (9.7)	4 (33)	8 (66)	0.130

(HTN- Hypertension, DM- Diabetes Mellitus, IHD- Ischemic Heart Disease, TIA- Transient Ischemic Stroke, CKD- Chronic Kidney Disease)

The above table shows the data of study population, their co-morbidities and comparison between both survived and not survived groups. Among 124 patients, 78 (62.9%) patients had HTN, out of them 37 (47%) survived and 41 (52%) died. DM was associated in 38 (30.6%) patients, in those 18 (47%) survived and 20 (52%) did not survive. Patients with IHD were 21 (16.9%); out of those 11 (52%) survived and 10 (47%) died in the hospital. Patients who were having previous stroke history and TIA were 22 (17.7%), among them 7 (31%) survived and the remaining 7 (31%) died. Twelve (9.7%) patients had CKD, out of those 4 (33%) survived and 8 (66%) didn‘t survive. The Chi square test was used to compare the comorbidities between survivors and non-survivors. Among all the comorbidities, previous H/O of stroke or TIA was significantly (**p=0.021**) associated with mortality in critically ill stroke patients.

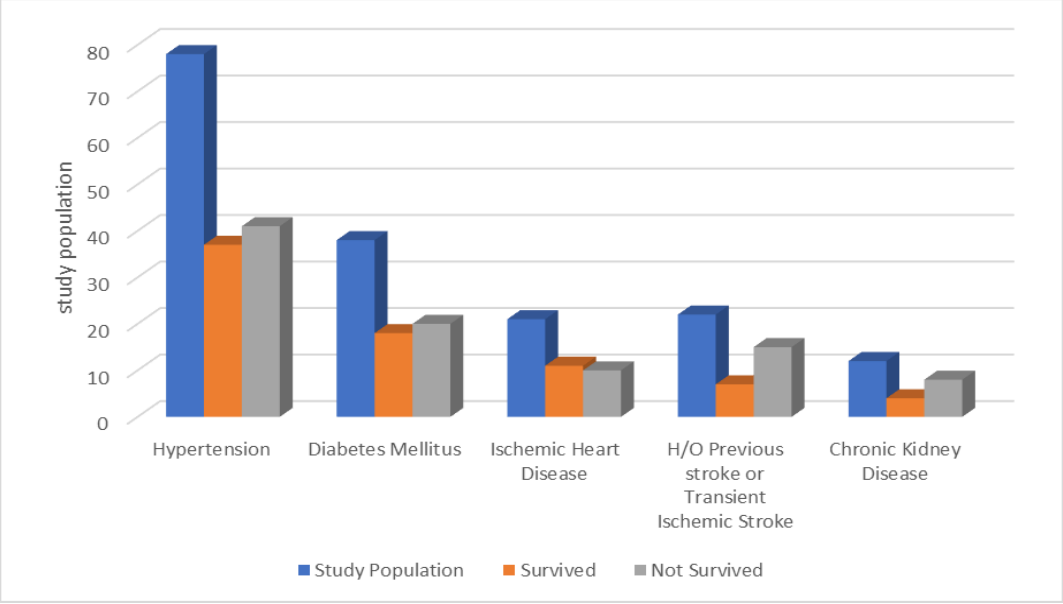


Figure 13: Number of patients with different comorbidities status in study population, survivors and non-survivors.

Table 9: Distribution of study population as well as both groups according to medication history and comparison of medication history between both groups

Medications	Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	p-value
Anti-Hypertensive	71 (57.3)	32 (45)	39 (55)	**0.02**
Oral-Hypoglycaemic	25 (20.2)	13 (52)	12 (48)	0.62
Insulin	11 (8.9)	5 (45)	6 (55)	
Anti- Coagulants/ Anti- Platelets	26 (21)	13 (50)	13 (50)	0.64
Lipid Lowering	30 (24.2)	12 (40)	18 (60)	0.07

The above table shows the distribution of study population according to medication history. Among 124 patients 71 (57.3%) were using anti-hypertensive medications in those 32 (45%) survived and 39 (55%) died. Patients who were using oral hypoglycemic agents were 25 (20.2%), in those 13 (52%) survived and 12 (48%) did not survive. Twenty six patients were on oral anti- coagulants or anti- platelets, in those 13 (50%) survived and 13 (50%) died. Patients on lipid lowering agents were 30 (24.2%), in those 12 (40%) survived and 18 (60%) died. The Chi square test was used to compare the medication history between survivors and non-survivors. Among all medications, use of antihypertensives was significantly (p=0.02) associated with mortality in critically ill stroke patients.

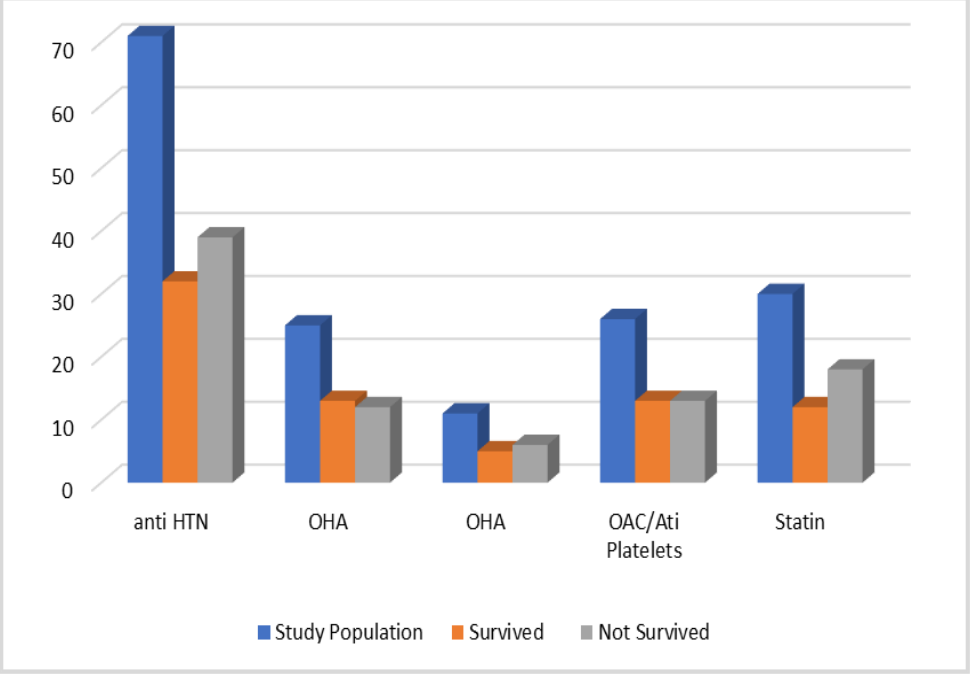


Figure 14: Number of patients with different medications in study population, survivors and non-survivors.

Table 10: Distribution of study population as well as both groups according to presenting vitals and comparison of presenting vitals between both groups

Vitals	Study Population (n=124)	Survived (n=67)	Not Survived (n=57)	Median Diff (95% CI)	p-value
HR (bpm)	89 (68, 106) (50-148)	89 (76, 104) (56-127)	89 (62, 113) (50-148)	0 (-5.9 to 9.8)	0.56
SBP (mmHg)	146 (126, 173) (79-240)	146 (128, 170) (92-230)	146 (120, 180) (79-240)	0 (-11.3 to 11.0)	0.99
DBP (mmHg)	85 (68, 104) (40-151)	89 (72, 102) (50-151)	81 (61, 106) (40-142)	7 (-2.12 to 13.6)	0.16
MAP (mmHg)	100 (84, 112) (62-186)	101 (90, 116) (62-177)	95 (77, 112) (56-186)	6 (-2.36 to 15.0)	0.18
SpO2 (%)	99 (98, 100) (93-100)	99 (98, 99) (94-100)	99 (98, 100) (93-100)	0 (-0.62 to 0.47)	0.31
RR (per min)	16 (14, 16) (12-28)	15 (14, 16) (16-28)	16 (14, 16) (12-128)	1 (-1.29 to 0.6)	0.23
Temp (○F)	98.5 (98.3, 99.5) (96.5-101.3)	98 (98.3, 98.9) (97.6-101.3)	98.5 (98.3, 99.3) (96.5-100.2)	0.5 (-0.3 to 0.2)	0.97

[Data presented and Median (IQR) (range)]. (HR- Heart rate; SBP and DBP- Systolic and Diastolic Blood Pressure, MAP- Mean Arterial Pressure, SpO2- Peripheral Oxygen Saturation, RR- Respiratory Rate, Temp- Temperature).

The above table display presenting vitals at ICU admission in study population and comparison of presenting vitals between survivors and non-survivors. The median (IQR) (range) HR (bpm) in the study population, survivors and non-survivors was 89 (68, 106) (50-148), 89 (76, 104) (56-127) and 89 (62, 113) (50-148) respectively. The SBP (mmHg) was 146 (126, 173) (79-240), 146 (128, 170) (92-230) and 146 (120, 180) (79-240) respectively.

The DBP (mmHg) was 85 (68, 104) (40-151), 89 (72, 102) (50-151) and 81 (61, 106) (40-142) respectively. The MAP (mmHg) was 100 (84, 112) (62-186), 101 (90, 116) (62-177) and 95 (77, 112) (56-186) respectively. The peripheral oxygen saturation (%) was 99 (98, 100) (93-100), 99 (98, 99) (94-100) and 99 (98, 100) (93-100) respectively. The respiratory rate (per minutes) was 16 (14, 16) (12-28), 15 (14, 16) (16-28) and 16 (14, 16) (12-128) respectively. The temperature (○F) 98.5 (98.3, 99.5) (96.5-101.3), 98 (98.3, 98.9) (97.6-101.3) and 98.5 (98.3, 99.3) (96.5-100.2) respectively.

Mann Whitney U Test was applied to compare the presenting vitals at ICU admission between survivors and non-survivors which showed a median difference (95% CI) and p-value of 0 (-5.9 to 9.8) and 0.56 for HR, 0 (-11.3 to 11.0) and 0.99 for SBP, 7 (-2.12 to 13.6) and 0.16 for DBP, 6 (-2.36 to 15.0) and 0.18 for MAP, 0 (-0.62 to 0.47) and 0.31 for SpO2, 1 (-1.29 to 0.6) and 0.23 for RR and 0.5 (-0.3 to 0.2) and 0.97 for temperature. The vitals at ICU admission did not affect the survival of critically ill stroke patients.

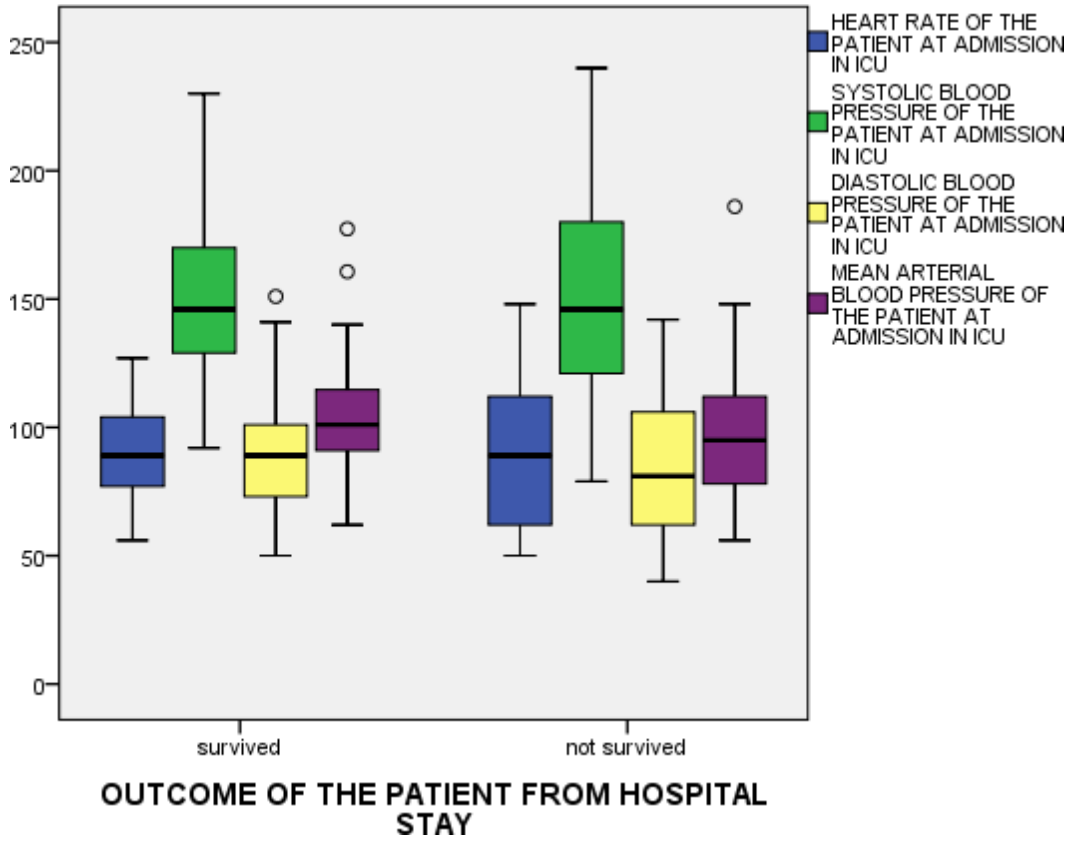


Figure 15: Box plot for comparison of median (IQR) (range) Heart rate, SBP, DBP, MAP between survivors and non-survivors.

Table 11: Distribution of study population as well as both groups according to different scores at presentation and comparison of different scores at presentation between both groups

Scores	Study Population (n=124)	Survived (n=67)	Not Survived (n=57)	Median Diff (95% CI)	p-value
GCS	9 (6, 11) (3-15)	11 (8, 15) (3-15)	6 (3, 8.5) (3-14)	5 (3.3 to 5.6)	**<0.001**
NIHSS	18 (10, 26) (1-36)	13 (8, 20) (1-34)	25 (17, 30) (4-36)	-12 (-12.2 to -6.4)	**<0.001**
APACHE II	18 (14, 21) (6-35)	14 (14, 18) (6-24)	21 (18, 24) (10-35)	-7 (-6.9 to -4.2)	**<0.001**
APACHE II AT 24 HOURS	18 (12, 22) (6-35)	14 (10, 16) (6-24)	22 (20, 24) (10-35)	-8 (-8.5 to -5.4)	**<0.001**

[Data presented and Median (IQR) (range)]. (GCS - Glasgow coma scale, NIHSS - National Institutes of Health Stroke Scale, APACHE II Acute Physiology and Chronic Health Evaluation II)

The above table displays different scores at ICU admission and at 24 hours in study population and comparison of these scores between survivors and non-survivors. The median (IQR) (range) GCS in the study population, survivors and non-survivors was 9 (6, 11) (3-15), 11 (8, 15) (3-15) and 6 (3, 8.5) (3-14) respectively. The NIHSS score was 18 (10, 26) (1-36), 13 (8, 20) (1-34) and 25 (17, 30) (4-36) respectively. The APACHE II score at admission was 18 (14, 21) (6-35), 14 (14, 18) (6-24) and 21 (18, 24) (10-35) respectively. The APACHE II score at 24 hours was 18 (12, 22) (6-35), 14 (10, 16) (6-24) and 22 (20, 24) (10-35) respectively.

Mann Whitney U Test was applied to compare the different scores at ICU admission and at 24 hours between survivors and non-survivors which showed a median difference (95% CI) and p- value of 5 (3.3 to 5.6) and <0.001 for GCS, 12 (-12.2 to -6.4) and <0.001 for NIHSS, 7 (-6.9 to -4.2) and <0.001 for APACHE II at admission and 8 (-8.5 to -5.4) and <0.001 for APACHE II at 24 hours. The GCS, NIHSS, APACHE II at admission and at 24 hours were significantly different between survivor and non-survivors i.e., lower GCS and higher

NIHSS, APACHE II at admission, and APACHE II at 24 hours was associated with mortality.

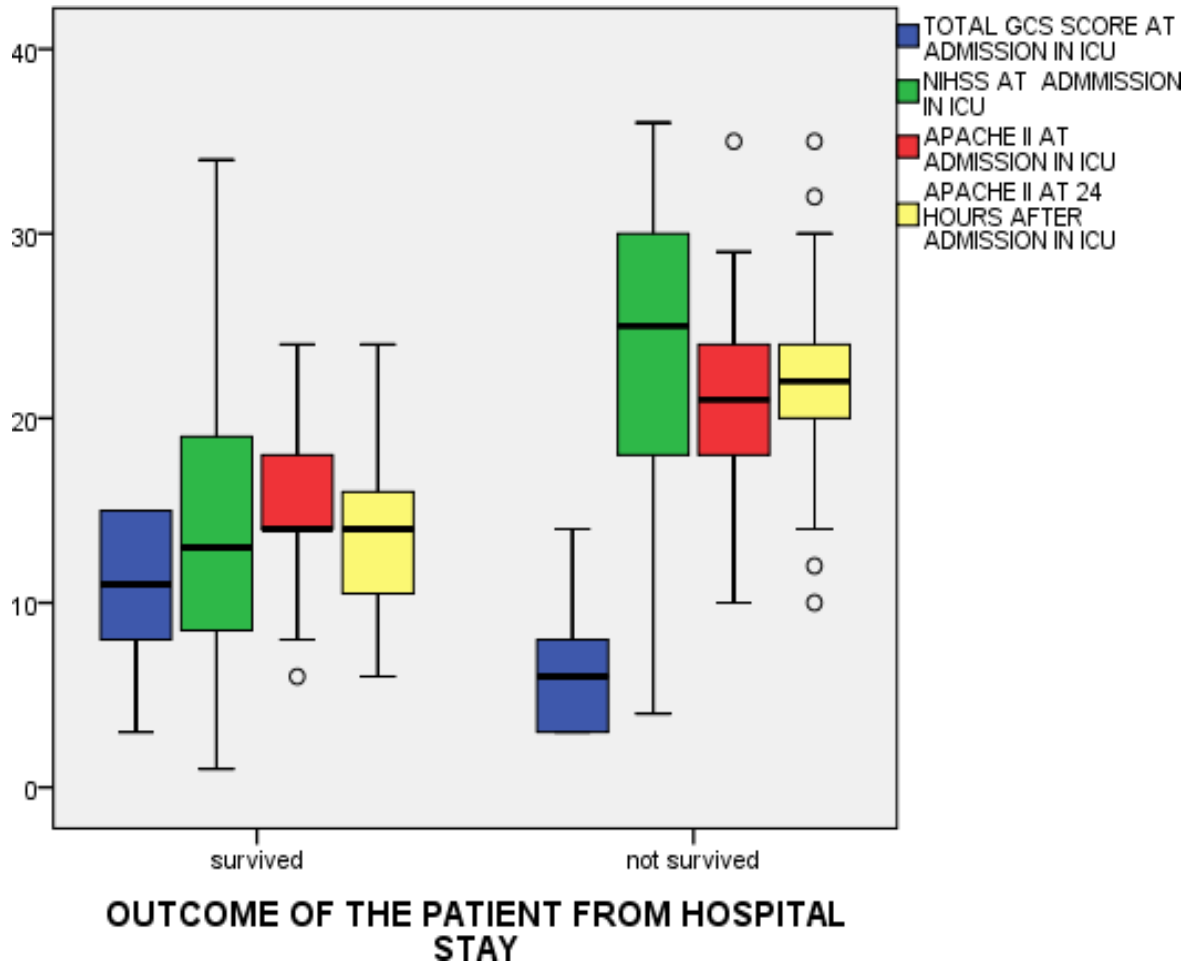


Figure 16: Box plot for comparison of median (IQR) (range) GCS score, NIHSS Score, APACHE II and APACHE II at 24hrs after admission in ICU between survivors and non-survivors.

Table 12: Distribution of study population as well as both groups according to investigation at presentation and their comparison between both group

Investigations		Study population (n=124)	Survived (n=67)	Not survived (n=57)	Median Diff (95% CI)	p-value
CBC	Hb (g/dl)	12.7 (10.2, 14.4)	12.7 (10.5, 14.8)	12.3 (10.1, 14.1)	0.4 (-2.2 to 1.9)	0.15
	WBC ($10^{\wedge 3}$/ul)	12.4 (8.9, 17.0)	11 (8.4, 14.8)	14.0 (11.0, 18.5)	3 (-5.5 to -0.4)	**0.006**
	NLR	8.6 (4.6, 15.2)	6.4 (2.1, 11.5)	12.1 (7.2, 17.8)	2.2 (-7.9 to -1.8)	**<0.001**
	PLR	0.2 (0.1, 0.4)	0.2 (0.1, 0.3)	0.3 (0.2, 04)	0.1 (-0.2 to -0.3)	**<0.001**
	Platelet	2.4 (1.6, 2.9)	2.4 (1.6, 2.9)	2.4 (1.6, 2.9)	0.1 (-0.4 to 0.3)	0.76
KFT	Urea (mg/dl)	36 (26.3, 59.5)	35 (23, 42)	40 (30, 82)	5 (-28.4 to -4.2)	**0.01**
	Cr (mg/dl)	1.1 (0.9, 1.5)	1.0 (0.8, 1.3)	1.2 (1.0, 2.5)	0.2 (-1.1 to -0.1)	**0.005**
LFT	SGOT (IU/L)	34.5 (22, 53)	32 (22, 48)	36 (22, 56)	4 (-28.1 to 23.6)	0.51
	SGPT (IU/L)	22.0 (14, 40)	22.0 (78,110)	22 (15, 40)	0.1 (-14.3 to 22.2)	0.90
	ALP (IU/L)	97 (81, 119)	96 (78-110)	100 (84, 132)	4 (-131.6 to 38.1)	0.22
	Tot. Bili (mg/dl)	0.6 (0.5, 0.9)	0.6 (0.5, 0.9)	0.6 (0.5, 0.8)	0.03 (-0.6 to 0.4)	0.97
	T.P (g/dl)	6.9 (6.1, 7.4)	6.8 (6.4, 7.2)	7.0 (5.6, 7.6)	0.2 (-0.2 to 0.5)	0.90
	Alb (g/dl)	3.7 (3.2, 4.1)	3.7 (3.3, 4.0)	3.7 (2.9, 4.2)	0 (-0.1 to 0.4)	0.65
	Glo (g/dl)	3.1 (2.8, 3.4)	3.1 (2.9-3.4)	3.2 (2.6, 3.5)	0.07 (-0.2 to 0.2)	0.85
	PT (sec)	15 (13.6, 16.3)	14.7 (13.7, 16.0)	15 (13.6, 17.1)	0.3 (-3.3 to 3.3)	0.68
	APTT (sec)	28 (25, 33.4)	28 (25, 32.8)	28.8 (25.0,34.6)	0.8 (-4.2 to 4.3)	0.54
	HBA1C (%)	6.1 (5.8, 6.8)	6.1 (5.7, 6.7)	6.1 (5.9, 7.2)	0 (-1.0 to 0.3)	0.22

[Data presented and Median (IQR) (range)]. (Hb - Haemoglobin, WBC- white blood cell count, NLR-Neutrophil Lymphocyte Ratio, PLR- Platelet lymphocyte ratio Cr- Creatinine,

Alb- Albumin, Glob - Globulin, Tot. Bili - total bilirubin, D. bili - direct bilirubin, T.P - total protein, HBA1C- glycosylated haemoglobin.)

The above table displays the data of study population's different investigations at admission and their comparison between both survivors and non-survivors. In CBC, the median (IQR) haemoglobin (g/dl) of study population, survived and not survived was 12.7 (10.2, 14.4), 12.7 (10.5, 14.8) and 12.3 (10.1, 14.1) respectively. The WBC count (10^{*3}/ul) was 12.4 (8.9, 17.0), 11 (8.4, 14.8) and 14.0 (10.92, 18.5) respectively. The NLR was 8.64 (34.59, 15.22), 6.36 (2.11, 11.5) and 12.1 (7.20, 17.8) respectively. The PLR was 0.21 (0.11, 0.38), 0.16 (0.08, 0.32) and 0.32 (0.17, 043) respectively. In KFTs, the median (IQR) urea (mg/dl) of the study population, survived and not survived was 36 (26.25, 59.50), 35 (23, 42) and 40 (30, 82) respectively. The creatinine (mg/dl) was 1.13 (0.85, 1.49), 1.01 (0.81, 1.32) and 1.20 (0.97, 2.50) respectively. In LFTs, the median (IQR) SGOT (IU/L) of the study population, survived and not survived was 34.5 (22, 53), 32 (22, 48) and 36 (22, 56) respectively. The SGPT (IU/L) was 21.95 (14, 40), 21.9 (78,110) and 22 (15, 40) respectively. The ALP (IU/L) was 97 (81, 119), 96 (78-110) and 100 (84, 132) respectively. The total bilirubin (mg/dl) was 0.6 (0.48, 0.88), 0.57 (0.46, 0.92) and 0.6 (0.49, 0.84) respectively. The albumin (mg/dl) was 3.7 (3.15, 4.10), 3.7 (3.34, 4.0) and 3.70 (2.88, 4.15) respectively. The globulin (mg/dl) was 3.1 (2.82, 3.43), 3.12 (2.9-3.40) and 3.19 (2.6, 3.54) respectively. The PT (sec) was 15 (13.6, 16.3), 14.7 (13.7, 16.0) and 15 (13.6, 17.1) respectively. The APTT (sec) was 28 (25, 33.4), 28 (25, 32.8) and 28.8 (24.95, 34.55) respectively. The median (IQR) HBA1C (%) was 6.1 (5.8, 6.77), 6.10 (5.70, 6.70) and 6.1 (5.9, 7.15) respectively.

Mann Whitney U test was applied to compare the different investigations at ICU admission between survivors and non-survivors which showed a median difference (95% CI) and p-value of 3 (-5.5 to -0.4) and 0.006 for WBC counts, 8 (-7.9 to -1.8) and <0.001 for NLR, 5 (-0.2 to -0.3) and <0.001 for PLR, 5 (-28.4 to -4.2) and 0.01 for urea, and 0.2 (-1.1 to -0.1) and 0.005 for creatinine. The WBC, NLR, PLR blood urea and serum creatinine at admission were significantly higher in non-survivors compared to survivor.

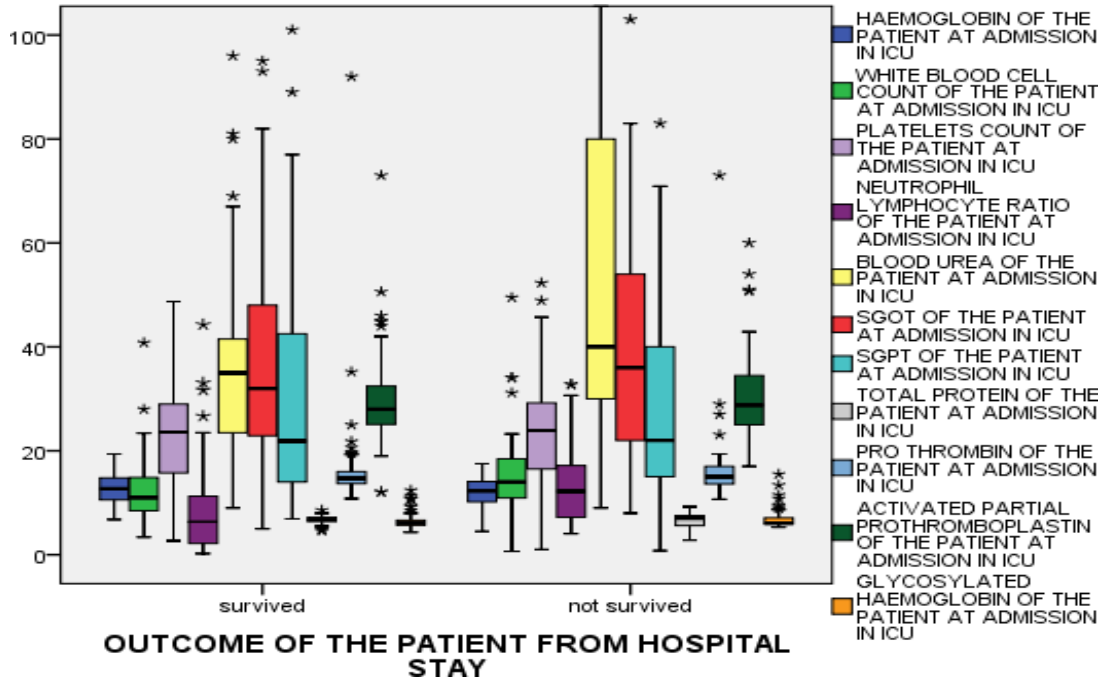


Figure 17: Box plot for comparison of median (IQR) (range) haemoglobin (gm/dl), TLC (1000/µL) and NLR, Platelet count (10000/µL), Urea (mg/dl), Creatinine (mg/dl), SGOT(IU/l), SGPT (IU/l), Total Protein , PT (Sec), APTT (sec) HbA1C (%) between survivors and non-survivors.

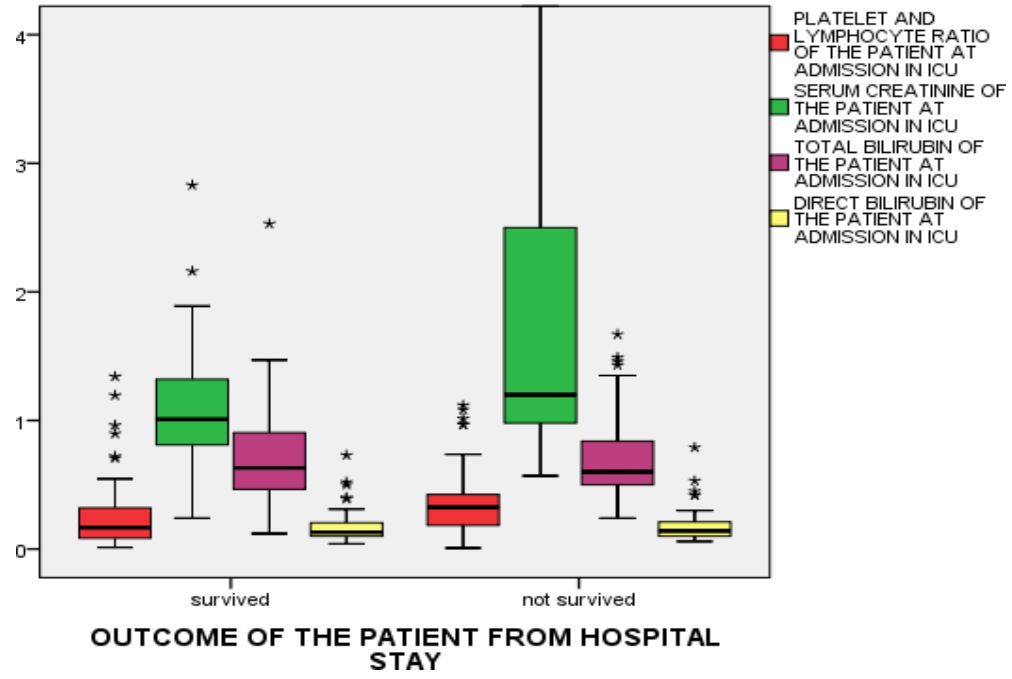


Figure 18: Box plot for comparison of median (IQR) (range) PLR, Serum Creatinine (mg/dl), Total Bilirubin (mg/dl), Direct Bilirubin (mg/dl), between survivors and non-survivors.

Table 13: Distribution of study population as well as both groups according to investigation (Lipid and Thyroid profile) at presentation and comparison of different investigations at presentation between both group

Investigations		Study population (n=124)	Survived (n=67)	Not survived (n=57)	Median Diff (95% CI)	p-value
Lipid Profile	HDL (mg/dl)	42 (33, 50) (3.62-158)	40 (32, 50) (3.62-158)	43 (34, 50) (8-69)	2 (-5.7 to 6.6)	0.542
	LDL (mg/dl)	91.5 (68, 117.3) (3.3-321)	93 (75, 118) (3.29-206)	84 (56.5, 114) (31-321)	1.5 (-15.3 to 19.6)	0.218
	Ch (mg/dl)	153.5 (109, 186) (14-466)	158 (118, 188) (24-466)	145 (108, 185) (14-131)	4.5 (-23.9 to 26.3)	0.524
	TG (mg/dl)	115 (85, 189) (39-1839)	115 (81, 204) (45-1839)	116 (90, 182) (39-1582)	0 (-47.7 to 129.8)	0.956
Thyroid profile	T3 (pg/ml)	1.51 (0.97, 2.0) (0.40-185)	1.69 (0.98, 230) (0.23-4.20)	1.26 (0.93, 1.79) (0.04 – 2.35)	0.18 (0.10 to 0.59)	0.12
	T4 (ng/dl)	1.03 (0.81, 1.23) (0.14-3.97)	1.09 (0.89, 1.30) (0.14-3.97)	0.96 (0.73, 1.09) (2.7 – 0.73)	0.06 (-6.4 to 18.9)	**0.005**
	TSH (mIU/l)	1.58 (0.78, 2.65) (0.009-8.60)	1.60 (0.82, 2.48) (0.3-7.25)	1.56 (0.7, 2.75) (0.009 - 8.6)	0.02 (-0.6 to 0.5)	0.823

[Data presented and Median (IQR) (range)]. (HDL- high density lipoproteins, LDL - low density lipoproteins, Ch - cholesterol, TG - Triglycerides, TSH - thyroid stimulating hormone)

The above table shows the data of study population‘s thyroid and lipid profile with its comparison between survivors and non-survivors. The median (IQR) (range) of the serum

HDL of study population, survived and not survived was 42 (33, 50) (3.62-158), 40 (32, 50) (3.62-158) and 43 (34, 50) (8-69) respectively. The serum LDL was 91.5 (68.0), 117.25) (3.29-321), 93 (75, 118) (3.29-206) and 84 (56.5, 114) (31-321) respectively. The serum cholesterol was 153.5 (109, 186) (14-466), 158 (118, 188) (24-466) and 145 (108, 185) (14-131) respectively. The serum triglyceride was 115 (85, 189) (39-1839), 115 (81, 204) (45-1839) and 116 (90, 182) (39-1582) respectively. The median (IQR) (range) of the serum T3 of study population, survived and not survived was 1.51 (0.97, 2.0) (0.40-185), 1.69 (0.98, 230) (0.23-4.20) and 1.26 (0.93, 1.79) (0.04–2.35) respectively. The serum T4 was 1.03 (0.81, 1.23) (0.14-3.97), 1.09 (0.89, 1.30) (0.14-3.97) and 0.96 (0.73, 1.09) (2.7–0.73) respectively. The serum TSH was 1.58 (0.78, 2.65) (0.009-8.60), 1.60 (0.82, 2.48) (0.3-7.25) and 1.56 (0.7, 2.75) (0.009-8.6) respectively.

Mann Whitney U Test was applied to compare the lipid and thyroid profile at ICU admission between survivors and non-survivors which showed a median difference (95% CI) and p-value of 2 (-5.72 to 6.6) and 0.542 for HDL, 1.5 (-15.3 to 19.6) and 0.218 for LDL, 4.5 (-23.9 to 26.3) and 0.524 for serum cholesterol, 0 (-47.7 to 129.8) and 0.956 for triglycerides, 0.18 (0.10 to 0.59) and 0.12 for serum T3, 0.06 (-6.43 to 18.9) and 0.005 for serum T4, and 0.02 (-0.57 to 0.53) and 0.823 for TSH. Among all, low serum T4 was significantly associated with mortality and affects survival of critically ill stroke patients.

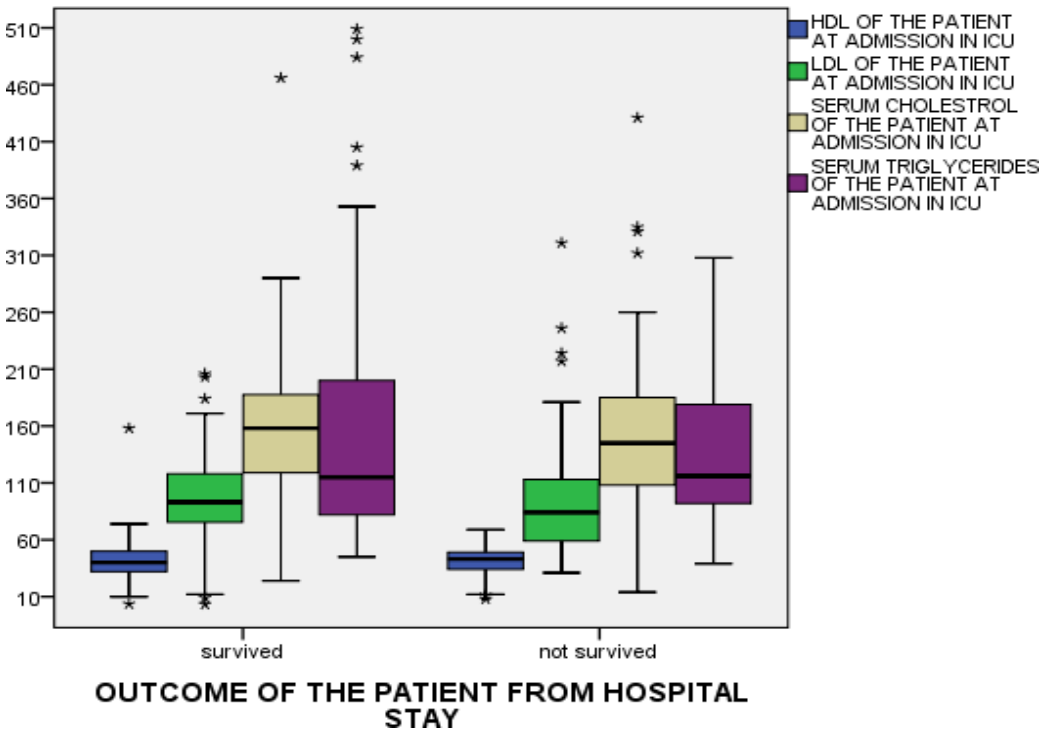


Figure 19 : Box plot for comparison of median (IQR) (range) HDL (mg/dl), LDL (mg/dl), Cholesterol (mg/dl) , Triglycerides (mg/dl), between survivors and non-survivors.

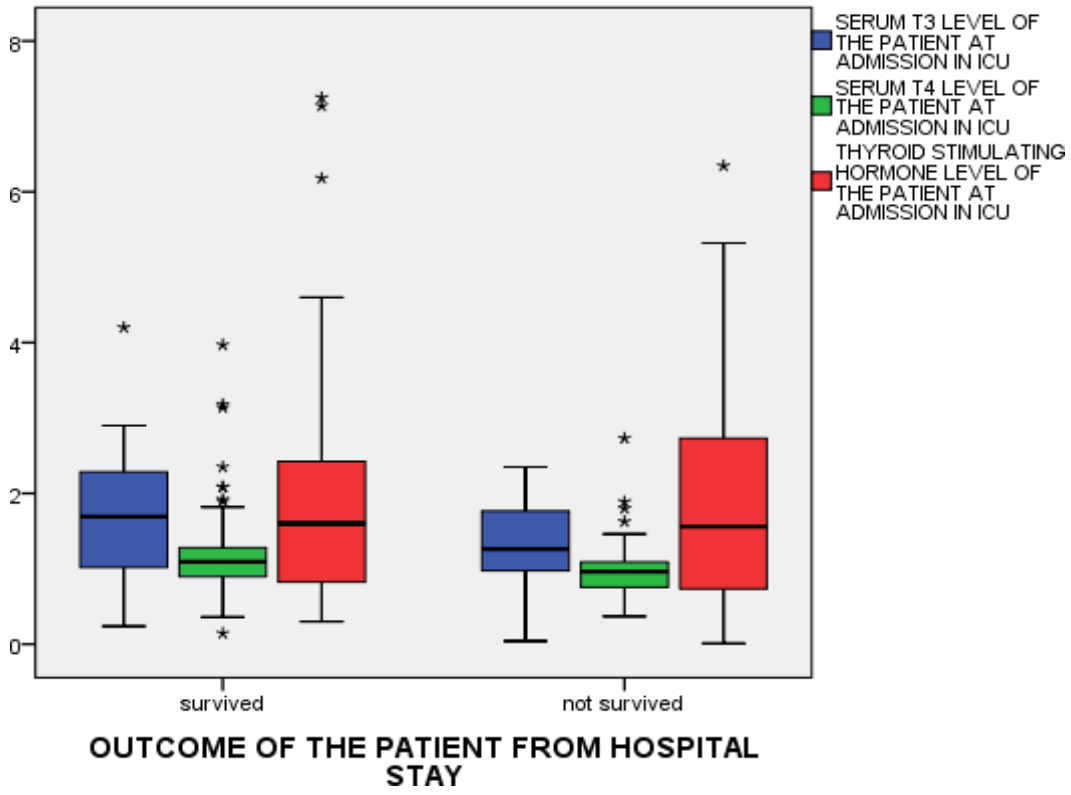


Figure 20: Box plot for comparison of median (IQR) (range) Serum T3(pg/ml), Serum T4 (ng/dl), TSH (mIU/l) between survivors and non-survivors.

Table 14: Distribution of study population as well as both groups according to investigation (Inflammatory Markers, Anticoagulants, Electrolytes) at presentation and comparison between both group

Investigation		Study population (n=124)	Survived (n=67)	Not survived (n=57)	Median Diff (95% CI)	p-value
IM	Hs-CRP (mg/l)	22.45 (5.63, 98.3)	20.69 (4.8, 123)	31.9 (5.65, 93.25)	11.21 (-18.3 to 26.6)	0.85
	IL-6 (pg/ml)	15.25 (2.74, 48.39)	12.79 (2.3, 36.86)	19.5 (4.04, 68.4)	6.71 (-115.7 to -2.92)	0.109
	d-dimer (ug/ml)	5.02 (1.54, 20)	3.69 (0.91, 20)	5.20 (2.23, 19.78)	1.51 (-13.5 to 53.6)	0.277
	Fibrinogen (mg/dl)	233 (186, 352)	234 (186, 347)	219 (174, 354)	15 (-40.9 to 55.0)	0.38
	Procalcitonin (ng/ml)	0.677 (0.235, 2.68)	0.675 (0.22, 1.98)	0.68 (0.31, 3.63)	0.005 (-5.31 to 12.1)	0.52
	Lactate (mmol/l)	1.56 (1.23, 2.35)	1.36 (1.09, 2.16)	1.78 (1.25, 2.40)	0.42 (-0.63 to 0.38)	**0.05**
	Ferritin (ng/ml)	182.19 (127, 276)	172 (96-263)	189 (156, 282)	17 (-311 to 19.3)	**0.04**
AC	Protein C (%)	66 (36, 84)	71 (42, 86)	61.3 (34, 80.2)	9.7 (-3.8 to 16.2)	0.15
	Protein S (%)	71.5 (45, 86)	76 (46, 92)	65 (31.5, 83)	11 (0.71 to 19.1)	**0.036**
	Anti-thrombin	71.65 (36.2, 94.7)	78 (40, 96)	51 (32, 90)	27 (-0.52 to 21.4)	**0.019**
	Homocysteine (umol/ml)	14.85 (12.3, 23.6)	15.63 (11.8, 21.8)	14.69 (12.5,25.4)	0.94 (-7.1 to 5.07)	0.93
E	Sodium (meq/l)	138 (134, 142)	137 (134, 142)	138 (134.5, 142)	1 (-2.6 to 1.7)	0.73
	Potassium (meq/l)	3.87 (3.44, 4.34)	3.89 (3.44, 4.37)	3.86 (3.47, 4.24)	0.03 (-0.2 to 0.3)	0.62

[Data presented and Median (IQR)] (IM-inflammatory markers, AC- anti-coagulants E-electrolytes)

The above table displays the data of study population‘s different investigations like inflammatory markers, serum anticoagulants and serum electrolytes with their comparison between survivors and non-survivors. The median (IQR) Hs-CRP of study population survived and not survived was 22.45 (5.63, 98.3), 20.69 (4.8, 123) and 20.69 (4.8, 123) respectively. The IL-6 of was 15.25 (2.74, 48.39), 12.79 (2.3, 36.86) and 19.5 (4.04, 68.4) respectively. The D-dimer was 5.02 (1.54, 20), 3.69 (0.91, 20) and 5.20 (2.23, 19.78)

respectively. The Serum Fibrinogen was 233 (186, 352), 234 (186, 347) and 219 (174, 354) respectively. The Procalcitonin was 0.677 (0.235, 2.68), 0.675 (0.223, 1.98) and 0.68 (0.31, 3.63) respectively. The Serum Lactate was 1.56 (1.23, 2.35), 13.6 (1.09, 2.16) and 1.78 (1.25, 2.40) respectively. The Serum Ferritin was 182.19 (127, 276), 172 (96-263) and 189 (156, 282) respectively. The Protein C was 66 (36, 84), 71 (42, 86) and 61.3 (34, 80.2) respectively. The Protein S was 71.5 (45, 86), 76 (46, 92) and 189 (156, 282) respectively. The Antithrombin was 71.65 (36.2, 94.7), 78 (40, 96) and 51 (32, 90) respectively. The Homocysteine was 14.85 (12.3, 23.6), 15.63 (11.83, 21.8) and 14.69 (12.55, 25.46) respectively. The Serum Sodium was 138 (134, 142), 137 (134, 142) and 138 (134.5, 142) respectively. The Serum Potassium was 3.87 (3.44, 4.34), 3.89 (3.44, 4.37) and 3.86 (3.47, 4.24) respectively.

Mann Whitney U test was applied to compare the inflammatory markers, serum anticoagulants and serum electrolytes at ICU admission between survivors and non-survivors which showed a median difference (95% CI) and p- value of 0.42 (-0.63 to 0.38) and 0.05 for serum lactate, 17 (-311 to 19.3) and 0.04 for serum ferritin, 11 (0.71 to 19.1) and 0.036 for protein S, and 27 (-0.52 to 21.4) and 0.019 for Antithrombin III. Among all different inflammatory markers, anticoagulants and electrolytes, higher serum lactate and serum ferritin levels and lower Protein S and Antithrombin III levels were significantly associated with mortality in critically ill stroke patients.

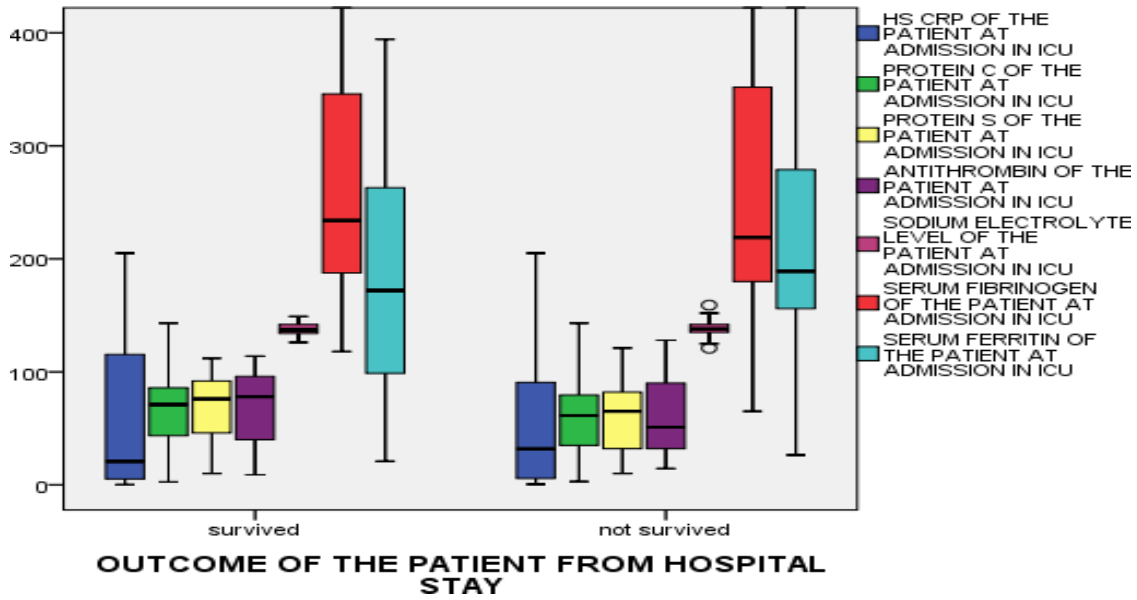


Figure 21 : Box plot for comparison of median (IQR) (range) hs- CRP (mg/l), protein C (%) , Protein S (%), Antithrombin (%), Sodium (meq/l) , Serum Fibrinogen (mg/dl), Serum Ferritin (ng/ml) level between survivors and non-survivors.

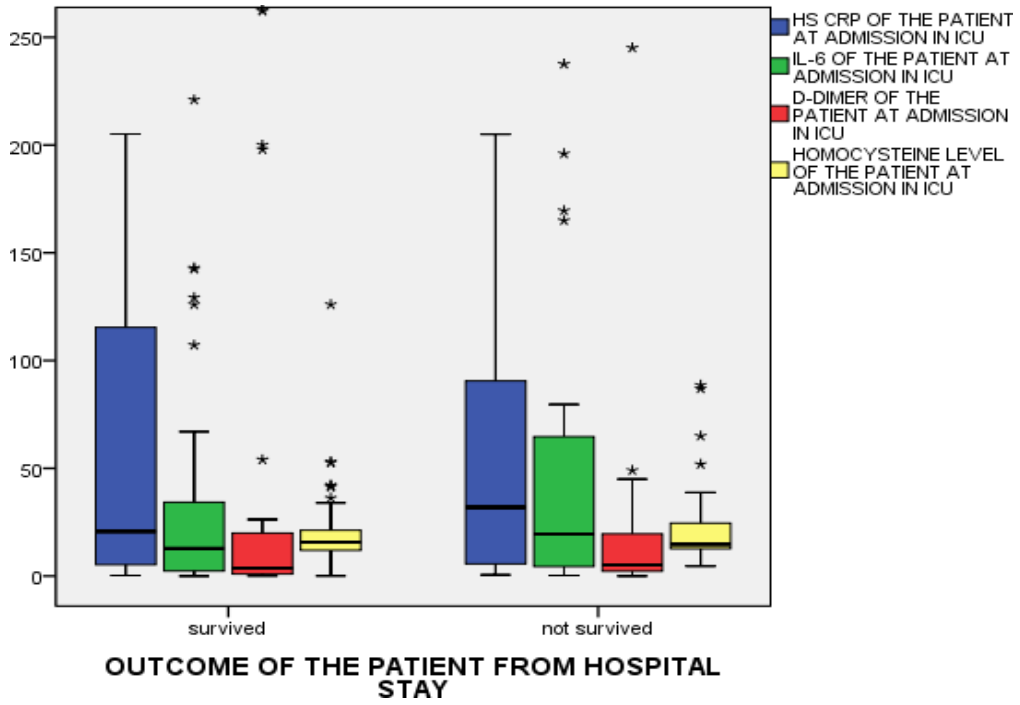


Figure 22 : Box plot for comparison of median (IQR) (range) IL-6 (ng/ml), d-Dimer (ug/ml), Homocysteine (umol/ml) level between survivors and non-survivors.

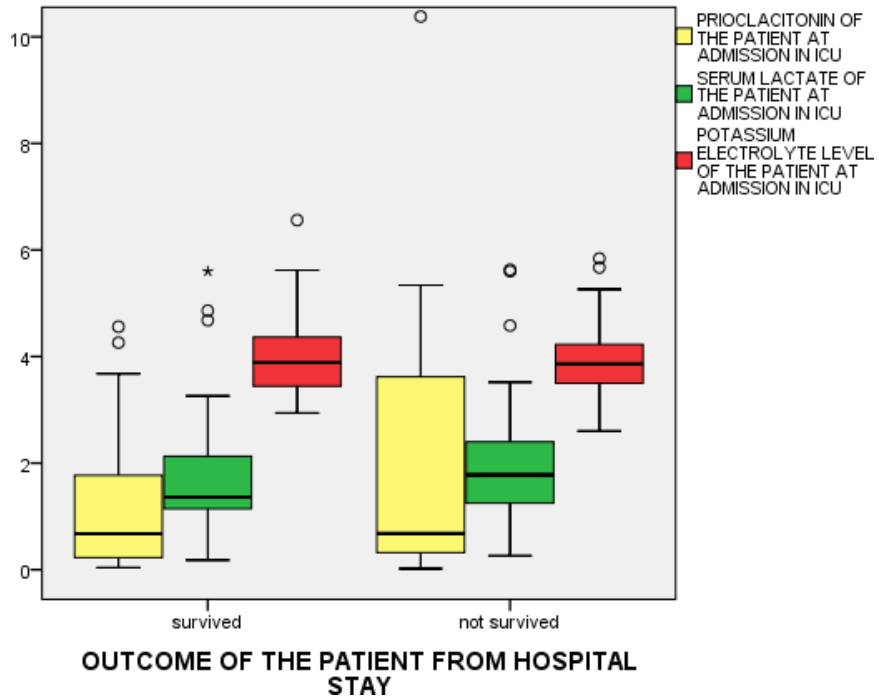


Figure 23: Box plot for comparison of median (IQR) (range) procalcitonin (ng/ml), Serum Lactate (mmol/l), potassium (meq/l) level between survivors and non-survivors,

Table 15: Distribution of study population as well as both groups according to stroke type and comparison of stroke type between both groups

Stroke Type	Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	p-value
Haemorrhagic Stroke	47 (37.9)	21 (31.30)	26 (58.6)	**0.03**
Acute Ischemic Stroke	77 (62.1)	46 (61.53)	31 (38.46)	

ICH was associated with higher relative risk of mortality [Odds ratio (95% CI) - 1.7 (1.6 to 2.7)]

The above table displays number and proportion as well as comparison of type of stroke (ischemic or hemorrhagic) among study population, survivors and non-survivors. Among 124 patients, 47 (37.1%) had hemorrhagic stroke, out of them 18 (31.3%) survived and 26 (58.6%) didn‘t survive. Remaining 77 (62.1%) patients had ischemic stroke, in them 46 (61.5%) survived and 31 (38.4%) did not survive. The Chi square test was used to compare the survival between both groups which showed a p value of 0.03, which was statistically significant i.e. Type of stroke affects survival of the critically ill stroke patients. Hemorrhagic stroke had higher relative risk [Odds ratio (95% CI) - 1.7 (1.05 to 2.7)] of mortality.

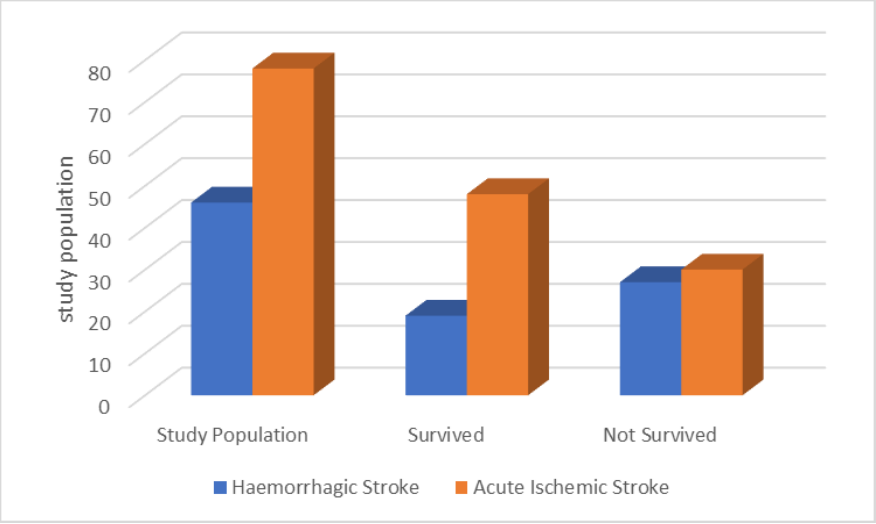


Figure 24: Number of patients with different types of strokes groups in study population, survivors and non-survivors.

Table 16: Distribution of study population as well as both groups according to subtypes of stroke at presentation and comparison of stroke subtypes between both group

Type of stroke		Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	χ^2; p-value
Acute ischemic stroke	Total anterior stroke	34 (27.4)	20 (29.9)	14 (24.6)	0.14
	Partial anterior stroke	21 (16.9)	15 (22.4)	6 (10.5)	
	Posterior circulation stroke	18 (14.5)	9 (13.4)	9 (15.8)	
	Lacunar stroke	4 (3.0)	2 (3.0)	2 (3.5)	
Intracranial haemorrhage	Intra parenchymal haemorrhage	43 (34.7)	21 (31.3)	22 (38.6)	
	SAH	4 (3.2)	-	4 (3.2)	

The data of the study population according to stroke subtype are shown in the above table, along with a comparison between both groups. Acute ischemic stroke was classified into subtypes according to the Bamford criteria. Total Anterior circulation stroke patients were 34 (27.4%) in those 20 (29.9%) survived and 14 (24.6%) did not survive. Partial Anterior circulation stroke patients were 21 (16.9%) in those 15 (22.4%) survived and 6 (10.5%) did not. 18 (14.5%) patients were diagnosed with posterior circulation stroke, in those 9 (13.4%) survived and 9 (15.8%) did not survive. Lacunar Stroke was diagnosed in 4 patients (3.0%) in those 2 (3.0%) survived and 2 (3.5%) did not survive. Total 47 patients had intracranial haemorrhage, in those patients with intraparenchymal haemorrhage were 43 (34.7%), out of them 21 (31.3 %) survived and 22 (38.6%) did not survive. 4 (3.2%) patients had SAH out of them none survived 4 (7%). Pearson's Chi Square test was applied for comparison of statistical significance and p-value was 0.14 which was statistically insignificant. Subtype of stroke did not affect the survival of critically ill stroke patients.

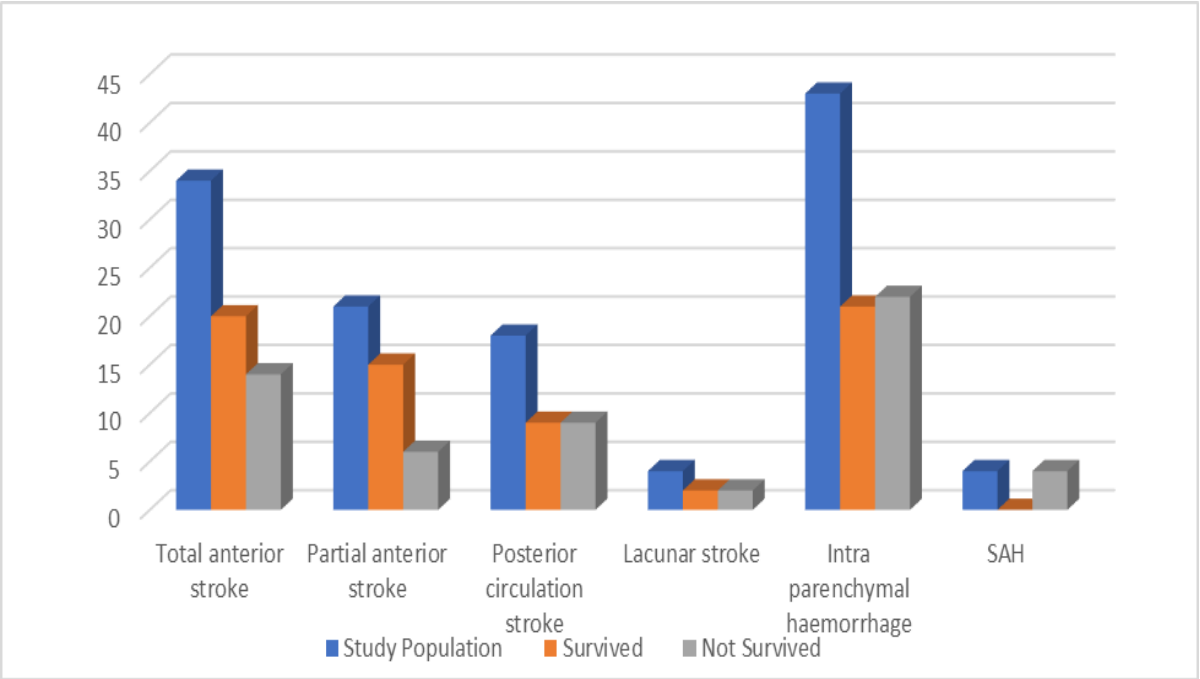


Figure 25: Number of patients with different types and sub types of strokes groups in study population, survivors and non-survivors.

Table 17: Distribution of study population as well as both groups according to specific ICU management and their comparison between both groups

ICU management		Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	χ^2; p-value
Conservative		58 (46.8)	34 (50.7)	24 (42.1)	1.90; 0.39
Medical (Alteplase)		32 (25.8)	18 (26.9)	14 (24.6)	
Surgical	Decompressive craniotomy	25 (20.2)	11 (16.4)	14 (24.6)	
	Ext Ventricular Drain (EVD)	9 (7.3)	4 (6.0)	5 (8.8)	

The above table shows the data of study population of stroke patients receiving different types of managements and comparison of management between survived and not survived groups. Among 124 patients, 58 (46.8%) were managed conservatively; in those 34 (50.7%) survived and 24 (42.1%) did not survive. 32 (25.8%) patients received Alteplase therapy, in those 18 (26.9%) patients survived and 14 (24.6%) died. Surgical management as decompressive craniotomy was received by the 25 (20.2%) patients; out of those 11 (6.4%) survived and 14 (24.6%) died. EVD was placed in 9 (7.3%) patients, in them 4 (6%) survived and 5 (8.8%) did not survive. Pearson's chi square test was applied to compare statistical significance, p-value was 0.39. Management did not affect survival of critically ill stroke patients.

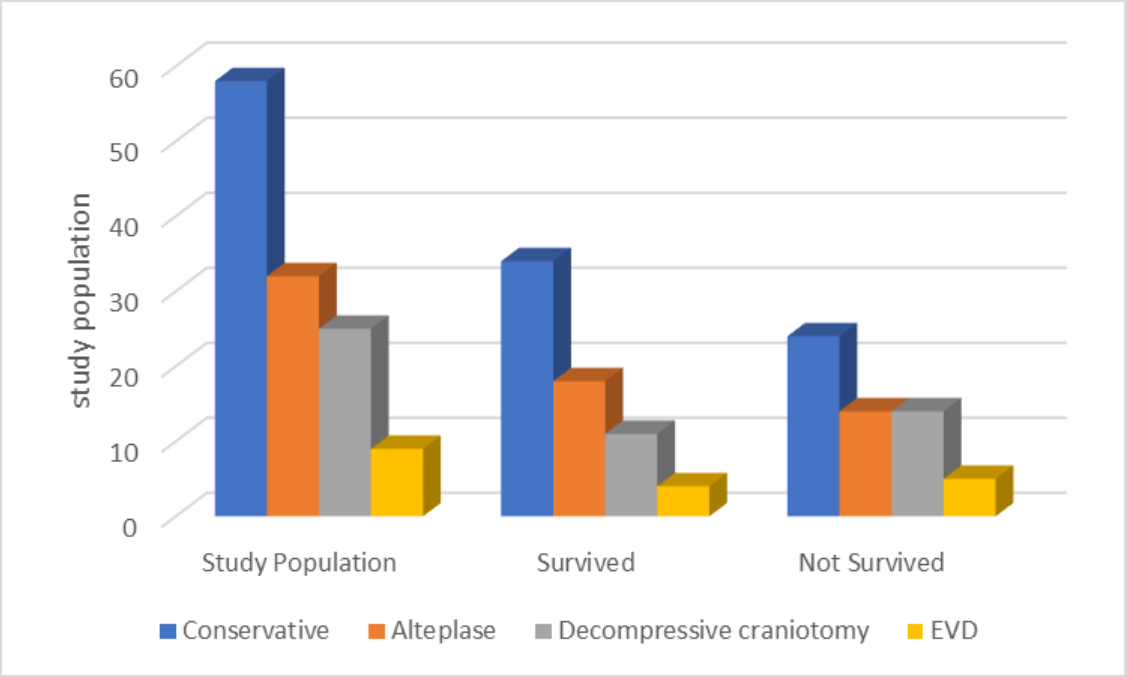


Figure 26: Number of patients with different types of ICU management received in the study population, survivors and non-survivors.

Table 18: Distribution of study population as well as both groups according to other management received and their comparison between both groups

Drugs		Study Population (n=124) (%)	Survived (n=67) (%)	Not Survived (n=57) (%)	χ^2; p-value
Vasoactive drugs	Received	56 (45.2)	23 (34.3)	33 (57.9)	**0.009**
	Not Received	68 (54.8)	44 (65.7)	24 (42.1)	
Other drugs	Received	29 (23.4)	12 (17.9)	17 (29.8)	0.248
	Not Received	95 (76.6)	55 (82.1)	40 (70.2)	
Mechanical Ventilation	Received	82 (66.1)	30 (44.8)	52 (91.2)	**<0.001**
	Not received	42 (33.9)	37 (55.2)	5 (8.8)	
Renal Replacement Therapy	Received	15 (12.1)	4 (6)	11 (19.3)	**0.023**
	Not received	109 (87.9)	63 (94)	46 (80.7)	

[Vasoactive drugs include Norepinephrine, Epinephrine, Nitro glycerine, and Labetalol. Other drugs include Propofol, Fentanyl, and Midazolam. Renal Replacement Therapy include Haemodialysis, and CRRT.]

The above table displays the data of study population as well as in both groups according to other management received during ICU stay. Total 56 patients received vasoactive drug infusion, out of them 23 (34.3) survived and 33 (57.9) did not survive. Mechanical ventilation was used on 82 (66.1) patients, in those 30 (44.8) survived, and 52 (82.1) died. Renal replacement therapy was received by 15 patients, in those 4 (6) survived, 11 (19.3) died. Pearson's Chi Square test applied to compare survival of patient between both groups and p-value for vasoactive drugs, mechanical ventilation and renal replacement therapy was <0.009, <0.001, 0.023 respectively which was statistically significant i.e, vasoactive drugs infusion, mechanical ventilation and renal replacement therapy received by the patient did have an effect on survival of critically ill patients.

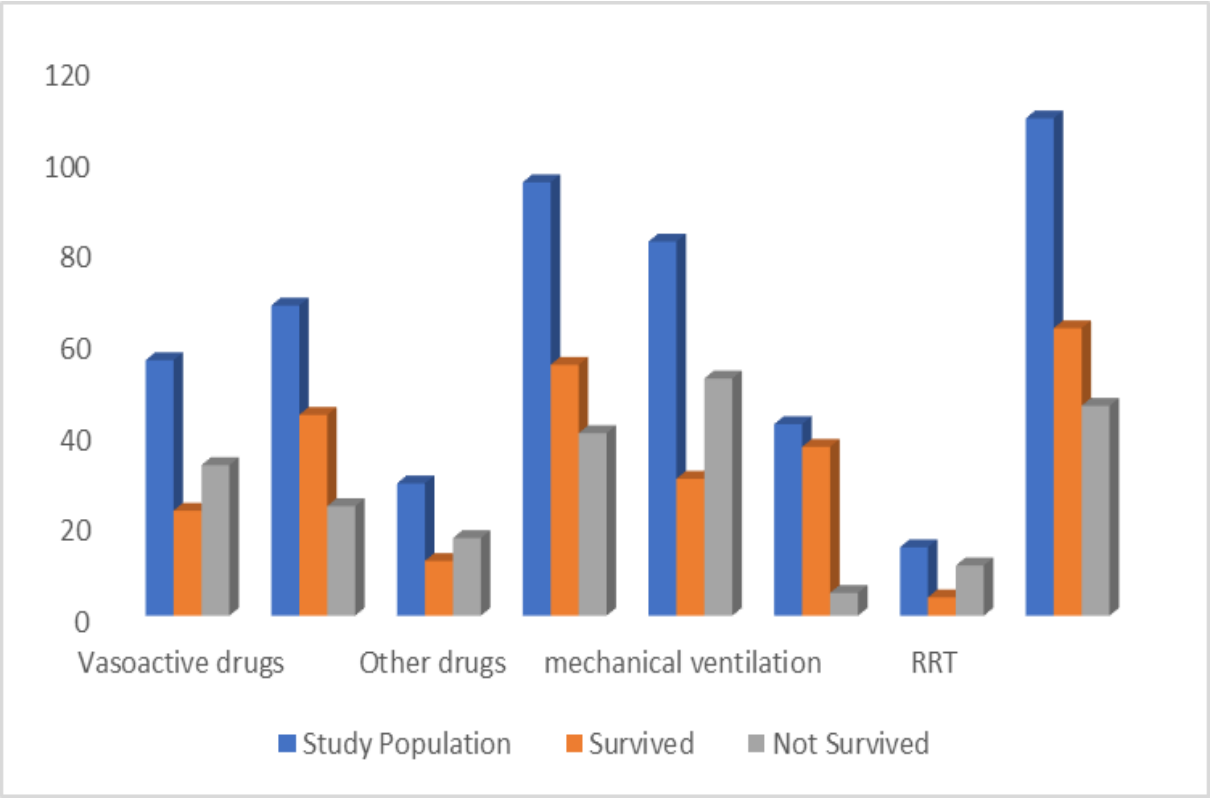


Figure 27: Number of patients according to other types of management received in the study population, survivors and non-survivors.

Table 19: Distribution of study population as well as both groups of ICU Stay and comparison of ICU stay between both groups

	Study population (n=124)	Survived (n=67)	Not survived (n=57)	Median Diff (95% CI)	p-value
Duration of ICU stay (days) [Median (IQR) (range)]	8 (3, 16) (1-44)	8 (4, 16) (1-38)	9 (2, 18) (1-44)	1 (-4.42 to 2.31)	0.554

The above table shows the median (IQR) (range) duration of ICU stay (days) in study population, survived and not survived groups. The ICU stay of study population, survivors and non-survivors was 8 (3, 16) (1-44), 8 (4, 16) (1-38) and 9 (2, 18) (1-44) respectively. Mann-Whitney U test was applied for comparison of survival between both groups and p-value was 0.554 which was statistically insignificant i.e., duration of ICU stay did not affect survival of critically ill stroke patients.

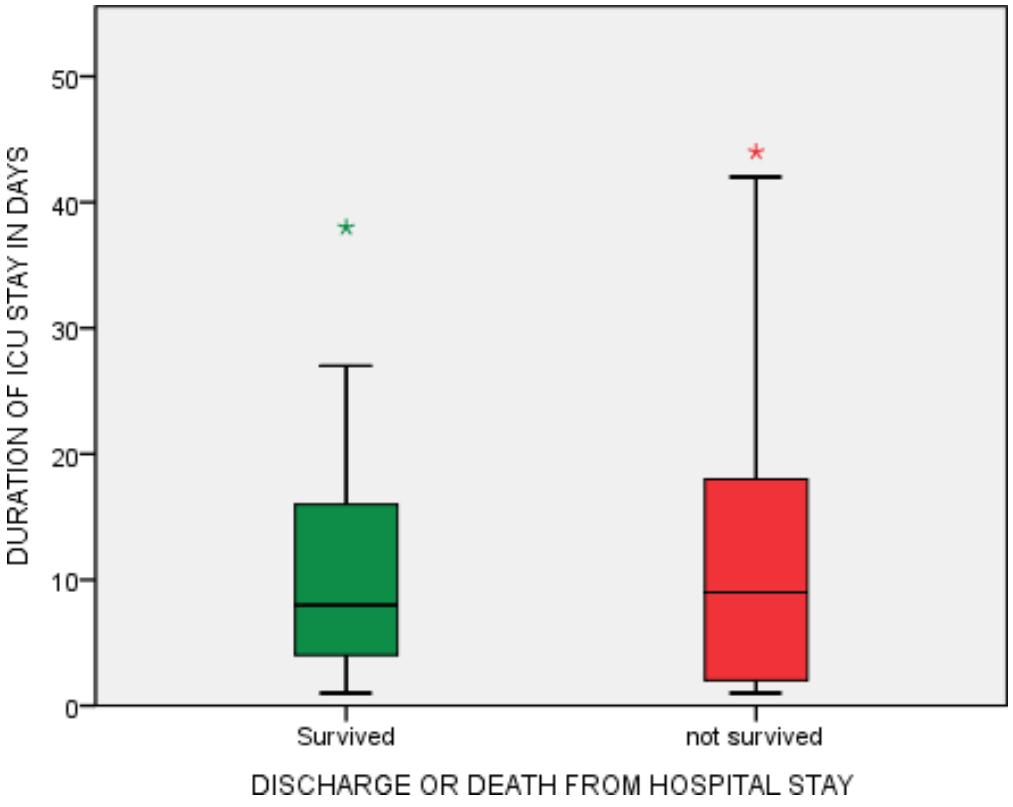


Figure 28: Box plot for comparison of median (IQR) (range) Duration of ICU stay between survivors and non-survivors.

Table 20 : Binary Logistic Regression Analysis output of all significant factors for predicting in hospital mortality of critically ill stroke patients

Parameter	Constant	Odds Ratio	95% CI	p-value
Previous history of TIA/ Stroke	-1.43	0.238	0.029 to 1.96	0.18
Antihypertensive	-0.90	0405	0.093 to 1.76	0.22
Type of Stroke	-0.02	0.979	0.16 to 5.99	0.98
GCS score	-0.12	0.884	0.66 to 1.18	0.40
NIHSS Score	0.088	1.092	0.97 to 1.22	0.126
APACHE II at admission	0.13	1.14	0.80 to 1.62	0.46
APACHE II at 24 hrs	0.24	1.34	1.07 to 1.7	**0.01**
WBC counts	0.06	1.06	0.93 to 1.21	0.37
NLR	-0.06	0.93	0.71 to 3.75	0.46
PLR	3.18	24.2	0.79 to 1.11	0.23
Blood Urea	-0.02	0.97	0.94 to 1.00	0.103
Serum Creatine	0.46	1.59	0.79 to 3.20	0.192
Serum T3	-0.55	0.57	0.19 to 1.73	0.325
Serum T4	-0.37	0.69	0.29 to 1.64	0.402
Serum Lactate	-0.26	0.77	0.38 to 1.53	0.45
Serum Ferritin	0.001	1.00	0.99 to 1.00	0.16
Protein S	-0.011	0.99	0.95 to 1.02	0.51
Anti-thrombin	-0.006	0.99	0.96 to 1.02	0.70
Vaso Active infusions	0.49	1.63	1.71 to 3.75	**0.024**
Mechanical Ventilation	2.66	14.63	1.78 to 115.5	**0.012**
Renal Replacement Therapy	-0.235	0.791	0.046 to 13.46	0.79

The binary logistic regression analysis was performed to find out whether the demographics, clinical and laboratory parameters could predict in-hospital mortality in critically ill stroke patients. The univariate logistic regression was applied to find out the parameters significantly associated with mortality. Among all the parameters previous history of TIA/ stroke, antihypertensive, type of stroke, GCS score, NIHSS Score, APACHE II at admission, APACHE II at 24 hrs, WBC counts, NLR, PLR, blood urea, serum creatinine, serum T3, serum T4, serum lactate, serum ferritin, protein S, anti-thrombin, and requirement of vaso

active infusions, mechanical ventilation, and renal replacement therapy were significantly associated with in hospital mortality in our study population. The collinearity between these parameters was excluded and parameters were subjected to binary logistic regression analysis for preparing a model for predicting in-hospital mortality.

Among the variables entered, APACHE II at 24 hrs, requirement of mechanical ventilation and requirement of vasopressor drug infusion showed statistical significance (p=0.01, 0.012 and 0.024 respectively). Interpretation from the table are as follows:

1. The log odds of in-hospital mortality of critically ill stroke patients requiring mechanical ventilation increases by 14.63 times compared to those not requiring mechanical ventilation.
2. The log odds of in-hospital mortality of critically ill stroke patients requiring vassopressor drugs infusion increases by 1.63 times compared to those not requiring vassopressor drug infusion.
3. For every one-unit increase in APACHE II at 24 hours, the log odds of in-hospital mortality increases by 1.34 or odds of mortality increases by 34%.

Table 21 : Binary Logistic Regression Analysis output of all significant factors for predicting 90-days mortality of critically ill stroke patients

Parameter	Constant	Odds Ratio	95% CI	p-value
Previous history of TIA/ Stroke	-1.15	0.315	0.029 to 3.38	0.341
Antihypertensive	-0.80	0.445	0.92 to 2.15	0.314
Type of stroke	-0.18	0.832	0.13 to 5.11	0.842
Sub type of stroke	0.48	1.628	0.81 to 3.23	0.16
GCS score	0.08	1.08	0.80 to 1.46	0.585
NIHSS Score	0.06	1.06	0.944 to 1.19	0.313
APACHE II	-0.13	0.88	0.60 to 1.28	0.50
APACHE II AT 24 HRS	0.58	1.79	1.22 to 2.64	**0.003**
WBC	0.042	1.04	0.92 to 1.17	0.50
NLR	-0.098	0.90	0.76 to 1.07	0.27
PLR	4.84	127	0.76 to 1.07	0.27
Blood Urea	-0.049	0.952	0.91 to 0.99	0.06
Serum Creatine	0.543	1.72	0.80 to 3.67	0.16
Serum T3	-0.93	0.39	0.133 to 1.16	0.09
Serum T4	-0.39	0.67	0.35 to 1.28	0.23
Serum Lactate	0.10	1.10	0.67 to 1.83	0.68
Serum Ferritin	0.002	1.00	0.99 to 1.00	0.34
Protein S	-0.018	0.98	0.95 to 1.01	0.28
Anti-thrombin	-0.004	0.90	0.76 to 1.07	0.27
Vaso Active infusions	0.90	2.47	1.04 to 5.87	**0.039**
Mechanical Ventilation	-2.41	11.1	1.67 to 74.2	**0.01**
Renal Replacement Therapy	-0.14	0.79	0.046 to 13.4	0.87

The binary logistic regression analysis was performed to find out whether the demographics, clinical and laboratory parameters could predict 90-day mortality in critically ill stroke patients. The factors which were found to be significantly associated with 90-days mortality with univariate analysis were subjected to binary logistic regression analysis for preparing a model for predicting 90-days mortality.

Among the variables entered, APACHE II at 24 hrs, requirement of mechanical ventilation and requirement of vasopressor drug infusion showed statistical significance (p=0.003, 0.01 and 0.039 respectively). Interpretation from the table are as follows:

1. The log odds of 90-days mortality of critically ill stroke patients requiring mechanical ventilation increases by 11.1 times compared to those not requiring mechanical ventilation.
2. The log odds of 90-days mortality of critically ill stroke patients requiring vasopressor drugs infusion increases by 2.47 times compared to those not requiring vasopressor drug infusion.
3. For every one-unit increase in APACHE II at 24 hours, the log odds of 90-days mortality increases by 1.79 or odds of mortality increases by 79%.

Table 22 : Distribution of study population's functional status at 90-days according to Barthel index

Barthel index score	Study population (n=58)	Percent
Score <20 or Total dependency	3	5.2
Score 21-60 or Severe dependency	22	37.9
Score 61-90 or Moderate dependency	32	55.2
Score >91 or Slight dependency	1	1.7

The above table displays data of study population who survived at 90 days according to Barthel index scale score classification. Out of 58 patients who survived after 3 months 3 (5.2%) patients were having total dependency, 22 (37.9%) patients were severely dependent, 32 (52.2%) were moderately dependent and, 1(1.7%) patient was slightly dependent.

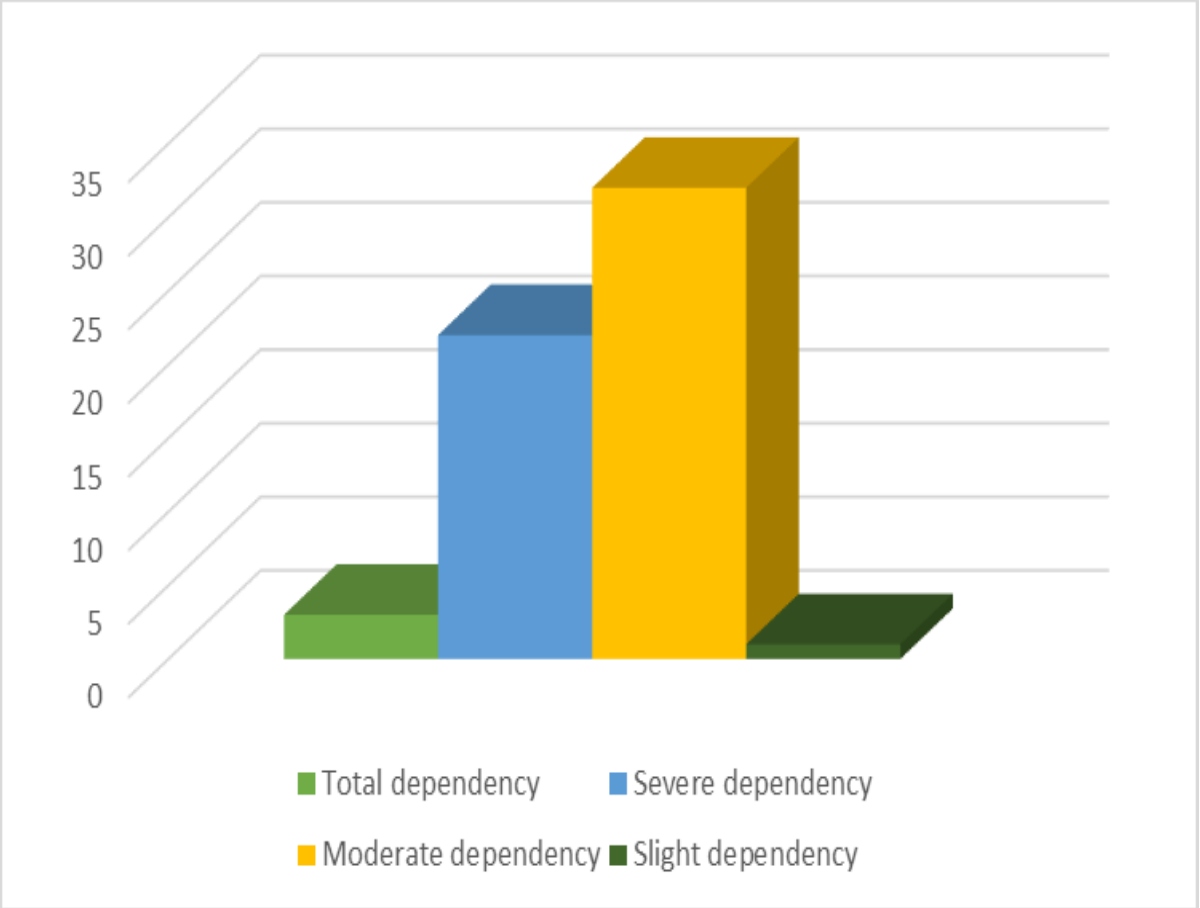


Figure 29: Distribution of study population's functional status at 90 days according to Barthel index score.

Table 23 : Distribution of study population' functional status at 90 days according to Modified Rankin scale

Modified Rankin Score at 90 days	Study population (n=124)	Percentage
Score 0-2 or No to Slight disability	19	15.3
Score 3-5 or Moderate to Severe disability	39	31.5
Score 6 or Dead	66	53.2

The above table displays the data of the study population's functional status at 90 days according to a modified rankin scale. Out of 124 patients, 19 patients had no to slight disability (MRS 0-2), 39 patients had moderate to severe disability (MRS 3-5), and 66 patients were dead (MRS 6).

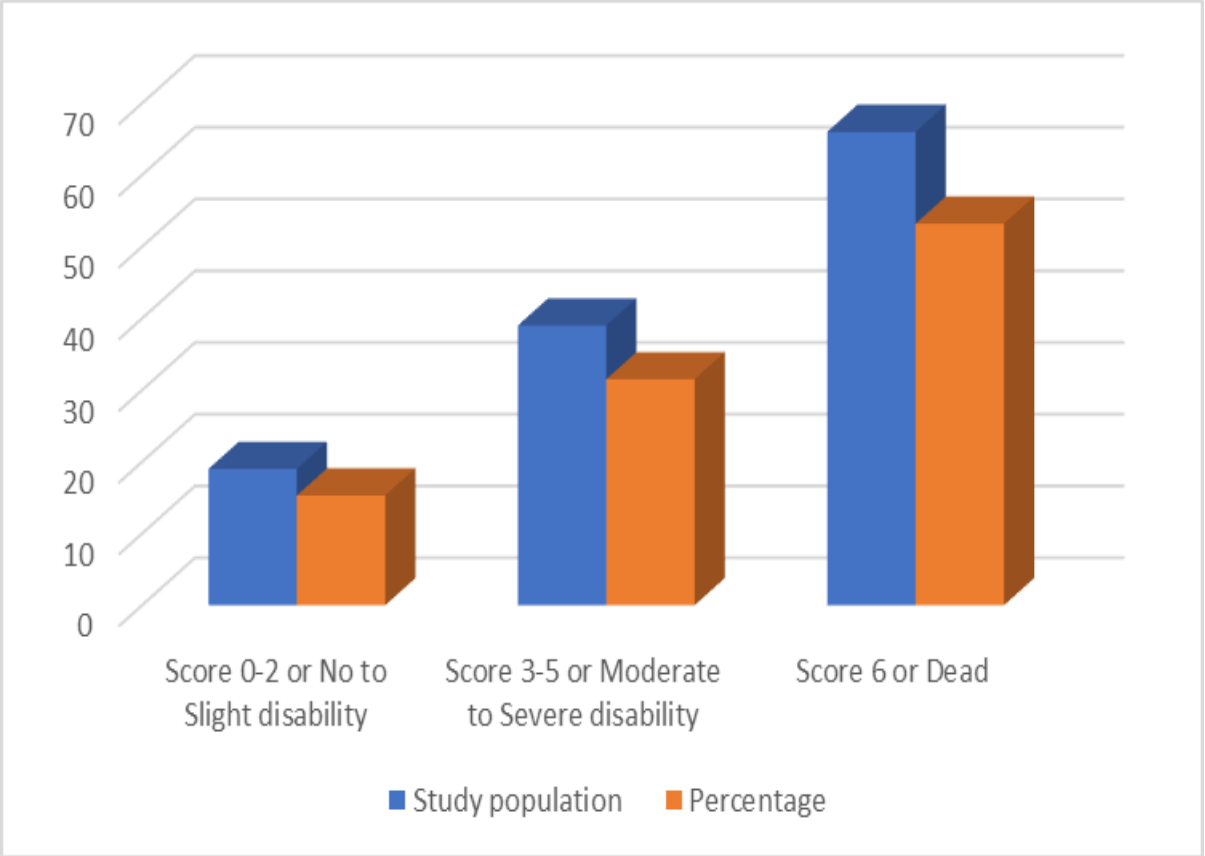


Figure 30: Distribution of study population who survived at 90 days according to Modified Rankin scale

DISCUSSION

The present study demonstrated that among critically ill stroke patients, around 50% expired within 90-days and more than half of those who survived beyond 90-days had moderate to severe functional limitation. Previous history of TIA/ stroke, antihypertensive use, type of stroke (ischemic or hemorrhagic), various scores [GCS, NIHSS, APACHE II (both at admission and at 24 hrs)], various investigations at admission (WBC counts, NLR, PLR, blood urea, serum creatinine, serum T3, serum T4, serum lactate, serum ferritin, protein S, anti-thrombin), and non-specific therapy (vasoactive infusions, mechanical ventilation, and renal replacement therapy) received during ICU stay were significantly associated with in hospital and 90-day mortality. The APACHE II at 24 hrs, requirement of mechanical ventilation and requirement of vasopressor drug infusion during ICU stay were independent predictors of in hospital and 90-day mortality among critically ill stroke patients.

The word ―stroke‖ was likely first introduced into medicine in 1689 by William Cole.[32] Before Cole, the common term used to describe non-traumatic brain injuries was ―apoplexy.‖ Apoplexy was used by Hippocrates circa 400 BC.[33] For >2000 years, physicians have struggled to define the term ―stroke.‖ In 1970, the World Health Organization defined stroke as ―rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.‖[34]

With an increase in life expectancy in India, there has been an increase in age-related, non-communicable diseases including stroke. The estimated incidence of stroke population in India varies from 116 to 163 per 100,000 population and its prevalence rate varies from 44.54 to 150/100000.[35] It is the fourth leading cause of death and fifth leading cause of disability adjusted life years (DALY).[36] During the acute phase of stroke, patients may require intensive care for various reasons, including altered mental status, seizures, medical complications (i.e., pneumonia, sepsis, hyponatremia) and for monitoring after neuroradiological or surgical procedures.

The accurate way to predict the likely long-term outcome (prognosis) for individual patients would help clinicians manage their patients and help relatives and patients come to terms with their changed circumstances. Clinicians can get some idea of their patients' likely outcomes by assessing simple clinical variables. Previous studies have examined predictors

of functional outcome or mortality in non-critical stroke patients and developed several predictive models; however, relatively few have been done on intensive care unit (ICU) admitted stroke patients.

The present study enrolled 124 critically ill stroke patients with the aim to find out association between various easily available patient data and outcome of critically ill stroke patients. The primary objective was to find out predictors of in-hospital mortality while secondary objectives were to find our predictors of 90-day mortality and functional status at 90-day.

Demographic Profile

Age:

In our study the median (IQR) age (years) for the study population, survivors and non-survivors was 60 (50, 70) (22-93), 60 (47, 69) (22-87) and 60 (50, 72) (23-93) respectively. We found that age of the patient did not affect survival of the critically ill stroke patients.

Similar to our finding, in a study conducted by de Montmollin et al. median (IQR) age (years) for the study population, survivors and non-survivors was 68.2 [57.9; 76.3], 67.2 [57.4; 74.8], and 69.1 [58.4; 76.9] respectively.[22] They did not find significant association of age with 1-year survival in critically ill stroke patients requiring mechanical ventilation. Moon et al. also found no significant difference in the age of study population (57.32 ± 17.24), survivors (54.28 ± 13.48) and non-survivors (59.22 ± 15.43).[29] They also found that age was not a an independent predictor of in hospital mortality in patients admitted to the intensive care unit (ICU) with acute stroke. However, a few other studies have found age to be an independent predictor of either in hospital or 1-year mortality in critically ill stroke patients.[28] The disparities in the results between published literature may be explained by the differences in the ethnicity of the population enrolled as well as varying sample size of the studies. However, age is a non-modifiable risk factor for stroke and has been shown to predict mortality in non-critically ill stroke patients. Therefore, further multicenter trials with larger sample size are required to establish the role of age in predicting mortality in critically ill stroke patients.

Other Demographic Variables:

In our study population, other demographic variables like gender, height, weight and BMI of the patients had no significant association with the mortality in critically ill stroke patients.

None of the previous studies conducted in critically ill stroke patients showed a significant association of gender, height, weight, and BMI of the patients and mortality. [22,28,29]

Socioeconomic status and Residential status:

In our study population, the socioeconomic status and residence (distance from hospital to residence of the patients) had no significant association with the in-hospital or after discharge mortality of the critically ill stroke patients. Published literature on the similar population of patients did not evaluated the role of these factors on mortality of the patients however, studies conducted in non-critically ill stroke patients had shown that the socioeconomic status and hospital distance from residence of the patients affect the in-hospital survival of the patients with lower socioeconomic status and longer distance from hospital was associated with higher mortality.[37] The observed difference is in-direct as these factors affects the onset of symptoms to treatment time (thrombolysis) and thereby the mortality of the patients.

Comorbidities:

In our study the most prevalent comorbidity was hypertension (62.9%) followed by diabetes mellitus (30.6%). Among all comorbidities, history of TIA or previous stroke was associated with significant mortality in our study population; however, it was not found to be an independent predictor in logistic regression. Previous studies also found hypertension as most prevalent comorbidity among critically ill stroke patients. [22,28,29] Similar to our findings, Alonso A et al. also found that the recurrent stroke was associated with significantly higher mortality; however, it was not an independent predictor of mortality among critically ill stroke patients.[28] In contrast, Fanshawe M et al. reported no significant association between previous stroke and mortality.[38] The disparity in the finding may be explained by the small sample size (n=61) of their study.

Medication History:

We compared the use of chronic medication between survivors and non-survivors and found that use of antihypertensive medication was associated with significantly higher mortality. Although it is an interesting finding; however, it is possible that the patient compliance to drugs may be different and those who survived might be more compliant to treatment. The history regarding the treatment compliance was not elicited. Previous studies in the similar study population did not evaluate the association of use of chronic medication and mortality in critically ill stroke patients.

Types and Subtypes of stroke:

In our study population, the most common type was ischemic stroke (n=77). Among them the most common subtype was total anterior circulation stroke followed by partial anterior circulation stroke. Remaining 47 patients had hemorrhagic stroke which include both intraparenchymal hemorrhage as well as subarachnoid hemorrhage. Haemorrhagic stroke had a significant association with higher mortality while subtype of stroke did not affect mortality. However, in regression analysis, type of stroke was not found to be an independent predictor of mortality. Similar to our finding, Alonso A et al. in their study enrolled 347 critically ill stroke patients, with around two third (72.6%) diagnosed with ischemic stroke and the remaining one-third (27.4%) diagnosed with intracerebral hemorrhage. They also found that hemorrhagic stroke was significantly associated with in-hospital mortality.[28] Various other studies on the similar subject failed to demonstrate type of stroke as an independent predictor of mortality.[29] In contrast, de Montmollin E et al. enrolled 419 critically stroke patients requiring mechanical ventilation with more than half (54%) diagnosed with hemorrhagic stroke and the hemorrhagic stroke was an independent predictor of survival at 1 year.[22] Carval T et al. also enrolled more than two third (76.8%) patients diagnosed as hemorrhagic stroke while less than one third (23.2%) as ischemic stroke.[19] They also found a significant association between hemorrhagic stroke and worst outcome (modified Rankin score) at sixth month.

Various Scores at admission in ICU:

In our study lower GCS, higher NIHSS and APACHE II score (both at admission and at 24 hours) was associated with mortality in critically ill stroke patients. Among these the APACHE II at 24 hours was an independent predictor of both in-hospital [Odds ratio (95% CI) 1.34 (1.07 to 1.7)] as well as 90-day [Odds raio (95% CI) 1.79 (1.22 to 2.64)] mortality. Similar results were found in study by Navarrete-Navarro P et al. where they reported significantly lower GCS and significantly higher APACHE III score in non-survivors (7.7±4.3 and 73.4±22.6 respectively) compared to survivors (9.6±4 and 55.8±29.9 respectively); however, only APACHE III was found be an independent predictor of in-hospital mortality in logistic regression.[13] Moon BH et al. also reported different scores in critically ill stroke patients. In their study the GCS in study population, survivors and non-survivors was 9.43 ± 4.18, 10.47 ± 3.95, and 6.49 ± 3.35 respectively (p-value <0.001); NIHSS was 21.63 ± 12.14, 19.08 ± 11.62, and 28.77 ± 10.66 respectively (p-value <0.001); APACHE II was 35.12 ± 23.73, 26.08 ± 17.84, and 49.77 ± 24.81 respectively (p-value

<0.001); and SAPS II was 35.34 ± 24.48, 25.90 ± 18.62, and 50.63 ± 25.15 respectively (p-value <0.001).[29] They also reported the mortality predictive ability of these scores using ROC curve analysis and found a slightly better prediction of mortality for APACHE II in hemorrhagic stroke and SAPS II in ischemic stroke patients. The GCS and NIHSS were inferior in predicting mortality in both patient groups.

In contrast, Carval T et al. in their study enrolled 323 patients with median (IQR) GCS of 6 (4-10) and found that higher GCS score was an independent predictor of good outcome (mRS<2) at 6-months.[19] de Montmollin E et al. also found that a lower GCS score at admission and a higher non-neurological SOFA score were independent predictors of decreased 1-year survival in critically ill stroke patients requiring mechanical ventilation.[22] They also evaluated the role of simplified acute physiology score (SAPS 2) and found it to be significantly different between alive and dead; however, it was not an independent predictor of 1-year survival. Alonso A et al. reported neurological status at admission using NIHSS and found that poor NIHSS score at admission was significantly associated with in-hospital mortality in acute stroke patients in need of intensive care treatment.[28] Jeng JS also reported that poor GCS and higher NIHSS at admission were independent predictors of 3-month mortality, 3-month mortality or institutional care, and poor functional outcomes at discharge in acute stroke patients admitted to the stroke intensive care unit.[12] Fanshawe M et al. also reported GCS <10 at admission as an independent predictor of increased mortality and poor functional outcome.[38]

Various Investigations at admission of ICU:

In our study routine investigations, inflammatory markers, anticoagulants and electrolytes were compared between survivors and non-survivors. Higher WBC counts, neutrophils lymphocytes ratio (NLR), platelets lymphocytes ratio (PLR), serum urea, serum creatinine, serum lactate and serum ferritin while lower serum T4, protein S, and antithrombin III were significantly associated with in-hospital and 90-day mortality in critically ill stroke patients. However, in regression analysis none of these investigations were found to be an independent predictor of mortality.

Ho WM et al. compared the laboratory investigations (CBC and KFT) between ischemic and hemorrhagic stroke as well as between survivors and non-survivors in critically ill stroke patients. WBC counts, and serum urea were significantly different between survivors and non-survivors in both ischemic and hemorrhagic stroke patients. Serum creatinine in hemorrhagic stroke and BUN/Cr ratio in ischemic stroke were significantly different between

survivors and non-survivors. In the logistic regression, WBC counts in ischemic stroke patients and serum creatinine in hemorrhagic stroke patients were independent predictors of mortality.[39]

Gebreyohannes EA et al conducted a study to evaluate mortality predictors among acuet ischemic stroke patients. They found that BUN [Odds ratio (95% CI) 1.020 (1.003-1.037)] and serum creatinine [Odds ratio (95% CI) 8.848 (1.616-67.437)] were significant predictors of mortality among patients with ischemic stroke.[40] Jeng JS also reported haematocrit <30% and WBC counts> $10^4/mm^3$ were independent predictors of 3-month mortality [Odds ratio (95% CI) 3.29 (1.71–6.34) and 1.70 (1.13–2.57) respectively], 3-month mortality or institutional care [Odds ratio (95% CI) 2.87 (1.17–7.06) and 1.82 (1.24–2.68) respectively], and poor functional outcomes at discharge [Odds ratio (95% CI) 4.37 (1.01–18.9) and 1.17 (0.77–1.78) respectively] in acute stroke patients admitted to the stroke intensive care unit.[12] Semerano A et al. in their study, found that good functional outcome was associated with a lower neutrophil to lymphocyte ratio (NL-R, OR 0.906 [95% CI 0.822-0.998]), a higher lymphocyte count (OR 1.547 [95% CI 1.051-2.277]), a higher eosinophil count (OR 1.027 [95% CI 1.007-1.048]), and a higher eosinophil to leukocyte ratio (EoLeu-R, OR 1.240 [95% CI 1.071-1.436]) at admission. Death within 3 months was associated with higher NL-R (OR 1.103 [95% CI 1.032-1.179]) as well as with lower eosinophil counts (OR 0.909 [95% CI 0.827-0.999]).[23]

Fettah Eren et al. studied lactate level and outcome of the patients with ischemic stroke and did not find significant association with outcome of the patient.[41] Nidin Mohan et al. studied only serum ferritin as a prognostic marker in stroke patients, they found that higher ferritin levels before 72 hours of ICU admission were associated with poor outcome of the patient with acute ischemic and hemorrhagic stroke.[42] In our study, serum lactate and ferritin levels were connected with patient survival outcome in univariate analysis, but no correlation was detected in multivariate regression analysis. It differs from earlier studies conducted on critically ill patients who already had high lactate levels from other causes like sepsis, severe hypotension, need for vasopressors etc, greater ferritin levels from other inflammatory disorders, or severe diseases or interventions. It could be one of the reasons why other inflammatory markers included in the study were not affecting the survival of critically ill patients.

A recent systematic review evaluated the prognostic role of hemostatic biomarkers including protein C, protein S, antithrombin III and d-Dimer, in acute ischemic stroke patients and concluded that none of the available hemostasis biomarkers are a predictor of clinical

outcome after acute ischemic stroke.[43] In a study by Zhang XG, levels of five common inflammatory markers including WBC count, NLR, serum CRP, and interleukin-6 (IL-6) were measured to identify independent predictors of outcome in stroke patients.[24] They found that NLR [Odds ratio (95% CI 1.13 (1.08 to 1.2)] and CRP [Odds ratio (95% CI 1.5 (1.24 to 1.82)] level were the best independent predictors of outcome.

ICU Management:

Stroke Specific Management-

In our study, 25% of patients with ischemic stroke who reached the hospital within 4 hours after the onset of symptoms got alteplase treatment. The majority (46%) of the patients were managed conservatively. Decompressive craniectomy was performed on 20% of the patients, while EVD was performed on 7% of the patients. The type of ICU management had no effect on stroke patient survival. The majority of patients with poor GCS were referred from different facilities received conservative management; nevertheless, the kind of ICU management had no impact on the survival rate of stroke patients.

Other non-specific Management-

We evaluated the role of other managements received in the ICU like vasoactive infusions, mechanical ventilation, renal replacement therapy etc. on mortality of critically ill stroke patients. The requirment of vasoactive drugs, mechanical ventilation and renal replacement therapy was significantly different between survivors and non-survivors. However, only vasoactive drug and mechanical ventilation requirement was found to be an independent predictor of in-hospital [Odds ratio (95% CI) 1.63 (1.71 to 3.7) and 14.63 (1.78 to 115.5) respectively] and 90-day [Odds ratio (95% CI) 2.47 (1.04 to 5.87) and 11.1 (1.67 to 74.2) respectively] mortality. Similar to our results Carval T et al. also found that requirement of mechanical ventilation was negatively [Odds ratio (95% CI) 0.09 (0.04–0.18)] associated with good neurological outcome (mRS 0-2) at 6 months in patients admitted to ICU with acute stroke.[19] Jeng JS et al. also found that mechanical ventilation requirement was independently associated with 3-month mortality [Odds ratio (95% CI) 5.61 (3.66–8.61)], 3-month mortality or institutional care [Odds ratio (95% CI) 13.6 (8.59–21.6)], and poor functional outcomes at discharge [Odds ratio (95% CI) 11.1 (5.45–22.4)].[12] Alonso A et al also reported that requirement of mechanical ventilation was associated with in-hospital mortality and poor outcome after rehabilitation.[28] Requirement of mechanical ventilation is an indirect indicator of poor GCS, respiratory failure, need for respiratory support in brain

death patients etc. therefore most studies reported its association with outcome of the critically ill.

In contrast, Pilato F et al. in their study on patients with acute ischemic stroke admitted to neuro-critical care unit failed to found a significant association of vasoactive drug infusions and mechanical ventilation with outcome at 3-months and 6-months. The difference in their study may be explained by their study population (patients who underwent intra-arterial mechanical thrombectomy alone or in combination with intravenous thrombolysis for acute ischemic stroke).[21] Perrine Bouvet et al. also assessed the role of vasopressor, mechanical ventilation and renal replacement therapy during ICU stay in patients with stroke. However, they did not find significant association of these therapies with long term functional outcome in critically ill stroke patients.[25]

Functional status at 90-days

In our study population, around one third (19 out of 58) of the patients had good functional outcome (mRS 0-2) at 90-days after hospital discharge. Other studies have also reported the percentage of patients having good functional outcome at 90-days mRS (0-2) and reported figures varies between 20%-50%. [19]

Study Strength

1. The present study evaluated the role of easily available data (demographics, clinical and laboratory) in predicting mortality among critically ill stroke patients.
2. We tried to include a variety of investigations such as inflammatory markers, anticoagulant profile, various types of neurological scores such as NIHSS, GCS, ICU scores such as APACHE II, various types of care and management received.
3. For assessment of functional outcome at 90-days, two commonly used scores (Barthel index and modified Rankin scale) were used.

Study Limitations

1. Since our study was an observational one, the bias that comes with trial design could not be ruled out.
2. We did not analyse ischemic and hemorrhagic stroke separately. Also, the origin of ischemic stroke (cardioembolic or atherosclerotic) was not separately evaluated.
3. We did not assessed long term outcome (at 6-months or 1-year).
4. The sample size was not calculated beforehand, hence the study may not have adequate power for a few results obtained. Therefore, further studies with adequate sample size are required to reciprocate the finding of our study.

CONCLUSION

Among critically ill stroke patients, previous history of TIA/stroke; use of anti-hypertensive; hemorrhagic type of stroke; higher NIHSS and APACHE II (both at admission and at 24 hours); higher WBC count, NLR, PLR, blood urea, serum creatinine, serum lactate, and serum ferritin; lower GCS, serum T4, protein S, and antithrombin III; and requirement of vasoactive drug infusion, mechanical ventilation and renal replacement therapy during ICU stay were significantly associated with in-hospital and 90-day mortality. The APACHE II score at 24 hrs, vasoactive drug infusion and requirement of mechanical ventilation during ICU stay were independent predictors of in-hospital and 90-day mortality for critically ill stroke patients. Around one-third of those who got discharged from hospital had a good functional outcome at 90-days after hospital discharge.

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ANNEXURE I

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/3494 **Date: 12/03/2021**

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3329**

Project title: **"Predictors of outcome in critically ill patients with stroke: A prospective observational study"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**M.D. Dissertation**
Student Name:	**Dr. Venkata Akhil Kasina**
Guide:	**Dr. Sadik Mohammed**
Co-Guide:	**Dr. Pradeep Bhatia, Dr. Samhita Panda, Dr. Bharat Paliwal & Dr. Rakesh Kumar**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

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E-mail : ethicscommittee@aiimsjodhpur.edu.in; ethicscommitteeaiimsjdh@gmail.com

ANNEXURE II

(Informed Consent Form)

TITLE: PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS WITH STROKE: A PROSPECTIVE OBSERVATIONAL STUDY

Name of PG Student: Dr. VENKATA AKHIL

Telephone no: 8328542816 Patient Identification No: _____

I,_____,g/o,r/o,s/o/d/o,_____r/o _____ _____ give my full, free, voluntary consent for my patient to be a part of the study –**Title**: **PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS WITH STROKE: A PROSPECTIVE OBSERVATIONAL STUDY'**‖ the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions. I understand that my patient's participation is voluntary, and I am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about my patient and any of my patient's medical records may be looked at by responsible individuals from AIIMS Jodhpur or from regulatory authorities. I give permission for these individuals to have access to my patient's records. I also give my consent for publication of my medical data for scientific and academic purposes.

Date:_____ _____

Place: _____ Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date : _____ _____

Place : _____ Signature of PG Student

1. Witness 1
   Signature
   Name:_____
   _____
   Address :_____

2. Witness 2
   Signature
   Name:
   Address : _____

ANNEXURE III

अखिल भारतीय चिकित्सा विज्ञान संस्थान, जोधपुर, राजस्थान
सूचित सहमतिप्रपत्र

थीसिस / निबंधकाशीर्षक: **PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS WITH STROKE: A PROSPECTIVE OBSERVATIONAL STUDY'**

पीजी छात्र का नाम: डॉ वेंकटा अखिल कसिना रोगी / स्वयंसेवकपहचानसंख्या: _____

नं..**8328542816**

मैं,_____एस/ओयाडी/ओ_____आर/ओ_____

_____

मेरे मरीज़ के लिए " **PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS WITH STROKE: A PROSPECTIVE OBSERVATIONAL STUDY'."**अध्ययन का हिस्सा बनने के लिए मेरी पूर्ण, नि: शुल्क, स्वैच्छिक सहमति देता/देती हूँ |

मेरी पूर्ण संतुष्टि के लिए मेरी भाषा में प्रक्रिया और प्रकृति को मुझे समझाया गया है।मैं पुष्टि करता हूं कि मुझे प्रश्न पूछने का अवसर मिला है। मैं समझता हूं कि मेरी मेरे मरीज़ की भागीदारी स्वैच्छिक है और मुझे किसी भी कारण दिए बिना किसी भी समय मेरे मरीज़ को अध्ययन से बाहर निकलने के मेरे अधिकार की जानकारी है। मैं समझता हूं कि मेरे मरीज़ के मेडिकल रिकॉर्ड के बारे में एकत्रित की गई जानकारी को _____ (कंपनी नाम) या विनियामक प्राधिकरणों से जिम्मेदार व्यक्ति द्वारा देखा जा सकता है। मैं इन लोगों के लिए मेरे मरीज़ के रिकॉर्डों तक पहुंच की अनुमति देता हूं। मैं इस बात की अनुमति देता हु की मेरे मेडिकल रिकार्ड्स को वैज्ञानिक और शैक्षिक प्रयोजनों के लिए इस्तेमाल किया जा सकता है

तारीख : _____.

जगह: _____ हस्ताक्षर / बाएं अंगूठे का छाप

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त की गई है

तारीख : _____

जगह: _____ पी जी छात्र के हस्ताक्षर

गवाह 1 गवाह 2

ANNEXURE IV

(Participant information sheet)

All India Institute of Medical Sciences Jodhpur, Rajasthan

All India Institute of Medical Sciences

Jodhpur, Rajasthan

Patient name:

Patient id:

Title of study: PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS WITH STROKE: A PROSPECTIVE OBSERVATIONAL STUDY'

Purpose of study: To find out association between patient characteristics, clinical features and laboratory values on day the day of admission to ICU, 30-day mortality and functional impairement at 90 days

Study design: Prospective Observational Cohort Study

I have been explained in my own understanding language by the Principal Investigator that they are doing this study and the risk and benefits associated with it.

I have been informed that I can withdraw my patient from the study at any time.

The data obtained from my patient will be used for the purpose of the study only. All records will be kept confidential.

Any potential risks to the participants: No additional risks

Details of the candidate with phone number: Dr. Venkata Akhil Kasina

Post Graduate, Anaesthesiology & Critical Care

AIIMS Jodhpur

ANNEXURE V

रोगी सूचना पत्रक

रोगी का नाम:

रोगी आईडी:

अध्ययन का शीर्षक: **PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS WITH STROKE: A PROSPECTIVE OBSERVATIONAL STUDY'**

अध्ययन डिजाइन: Prospective Observational Cohort Study

प्रिंसिपल अन्वेषक द्वारा मुझे अपनी समझ भाषा में समझाया गया है कि वे"ये अध्ययन कर रहे हैं और इसके साथ जुड़े जोखिमों और लाभों को भी समझाया गया है। मुझे सूचित किया गया है कि मैं किसी भी समय अध्ययन से मेरे मरीज़ को हटा सकता हूं। मेरे मरीज़ से प्राप्त आंकड़ों का उपयोग केवल अध्ययन के उद्देश्य के लिए किया जाएगा मेरे मरीज़ के सभी रिकॉर्ड गोपनीय रखा जाएगा।

प्रतिभागियों को कोई भी संभावित जोखिम: कोई अतिरिक्त जोखिम नहीं

डॉ वेंकटा अखिल कसिना
पीजी
अनेथीसिओलॉजी और क्रिटिकल केयर
एम्स जोधपुर
8328542816

ANNEXURE VI

Case Record Proforma

PATIENT STICKER

Age (yrs): _____ Gender: (Male / Female)

Height (cm): _____ BMI (kg/m^2):

DEMOGRAPHICS:

Name:_____

Weight (kg): _____

_____

Socioeconomic status**:** Rural/ urban: _____

	Date	Time
Symptoms Onset		
Admission to ED		
Admission to ICU		

CLINICAL MENIFESTATION:

_____

_____

DIAGNOSIS: Acute Ischemic Stroke/ Intracranial Haemorrhage/ Sub Arachnoid Haemorrhage

COMORBIDITIES: (Please mark)

Hypertension / Diabetes / asthma / tuberculosis / Dyslipidemia / Atrial Fibrillation / Previous Stroke / TIA / Previous MI / CAD / Illicit Drugs / Obesity / Sleep Apnoea / Chronic Kidney Disease/ Others (Please specify:_____).

DRUG HISTORY: **(Please mark)**

Oral Anticoagulants / Anti Hypertensives / Lipid Lowering Agents / Oral Hypoglycemic Agents/ Insulin / Other (Please specify:_____).

VITALS & OTHER SCORES at ICU ADMISSION:

HR (bpm): _____ BP (mmHg): SBP _____ DBP_____MAP_____

SPO2 (%): _____ RR (/min): _____ TEMP (^oC): _____

GCS at ICU Admission: EYE:_____VERBAL:_____MOTOR:_____TOTAL: _____

NIHSS SCORE at Admission ICU: _____

APACHE II at Admission ICU:_____ at 24 Hours: _____

LABORATORY DATA WITHIN 24 HOURS AFTER ICU ADMISSION:

Routine Investigation		Inflammatory Markers	
Haemoglobin (gm/dl)		Hs-CRP	
WBC (/µL)		IL-6	
N/L/E/B (%)		d-Dimer	
Blood Urea/S. Creatinine (mg/dl)		Serum fibrinogen	
SGOT/SGPT/ALP (IU)		Procalcitonin	
S. Bilirubin Total /Direct (mg/dl)		Serum lactate	
Total Protein/Albumin (mg/dl)		Serum Ferritin	
PT/INR/APTT		Protein C	
HbA1C (%)		Protein S	
HDL/LDL/VLDL (mg/dl)		Homocysteine	
S. Cholesterol/Triglycerides (mg/dl)		Antithrombin	
T3/T4/TSH		Lactate	

CT/MRI SCAN: Ischemic Stroke Subtype (Total Anterior Circulation Stroke / Partial Anterior Circulation Stroke / Lacunar Stroke / Posterior Circulation Stroke)

Impression: _____

_____

2-D Echo: _____

_____

ICU MANAGEMENT:

Thrombolysis / Surgical / Angiographic / Intravascular Procedures (Please specify _____)

Indication for and Duration of Mechanical Ventilation support: _____

Hypotensive and Vasoactive Drug Infusions:

_____

Other (Antiarrhythmic, Sedative, Relaxant): _____

Intraventricular Catheter or Lumbar Drain: _____

Indication for and Duration of Hemodialysis/CRRT: _____

Outcome: Discharge / Death

Duration of ICU Stay: _____

FOLLOW-UP at 3 MONTHS:

Outcome: Death / Survival with Institutional Care / Survival Living at Home

Modified Rankin score at 90 days:

Barthel index score at 90 days:

ANNEXURE VII MASTER CHART

DATE	NAME	AGE	GENDER	PATIENT ID	WEIGHT	HEIGHT	HEIGHT IN M	BMI	SOCIOECONOMIC STATUS	RURAL/URBAN	SYMPTOMS ONSET	ADMISSION TO ED	TIME TO ED in hrs
06/03/2022	KHUMAN SINGH	65	M	2022/03/003744	72	169	1.69	25.20920136	LOWER MIDDLE CLASS	URBAN	6/3/22 6:00AM	6/3/22 2:45PM	6
23/03/2022	Raghu Nath	42	M	2022/03/001418	88	169	1.69	30.8112461	UPPER CLASS	URBAN	23/03/2022	23/3/2211:23PM	5
03/04/2022	BABU LAL	62	M	2021/06/001387	78	172	1.72	26.36560303	LOWER MIDDLE CLASS	URBAN	03/04/2021 10:30	3/4/21 11:40AM	1
08/09/2021	DINESH KUMAR	60	M	2021/06/002783	90	172	1.72	30.42184965	UPPER MIDDLE CLASS	URBAN	08/06/2021 7:00AM	08/09/2021 12:30	04:20
13/02/2022	JAGMAL RAM	79	M	2022/02/007251	55	158	1.58	22.03172568	LOWER CLASS	RURAL	13/02/2022 09:00	13/2/22 10:30AM	0.45
08/02/2022	HARI OM MITTAL	75	M	2022/02/005509	82	165	1.65	30.11937557	UPPER MIDDLE CLASS	URBAN	08/02/2022 2:00PM	09/02/2022 11:00AM	8
07/06/2021	Manohar Singh	46	M	2021/ 06/00185	92	168	1.68	32.59637188	UPPER CLASS	URBAN	7/6/2021 10:00am	07/06/2021 12:00	01/01/1900 00:00
01/08/2021	REYAZ	50	M	2021/05/000361	62	162	1.62	23.62444749	UPPER MIDDLE CLASS	URBAN	01/05/2021 5pm	1/5/2021 7pm	0.45
23/06/2022	vikash	46	m	2022/03/017900	72	162	1.62	27.43484225	LOWER MIDDLE CLASS	RURAL	23/6/22 10:30am	23/6/22 1:00pm	4
03/04/2022	IMRATA	47	M	2022/06/002072	85	170	1.7	29.41176471	UPPER MIDDLE CLASS	RURAL	3/4/22 10pm	3/4/22 1:30pm	3
15/07/2022	Bhagirath ram	50	M	2022/07/010309	65	172	1.72	21.97133586	UPPER MIDDLE CLASS	URBAN	15/7/2022 8:00am	15/7/2022 11:00am	3
31/03/2021	CHANDMAL CHOPRA	61	M	2021/04/000595	62	168	1.68	21.96712018	UPPER CLASS	URBAN	21/03/2021 11:00	02/02/2021 12:30	48
13/03/2021	SUSHILA JOSHI	70	F	2022/03/010427	72	159	1.59	28.47988608	LOWER CLASS	URBAN	13/03/2021 10:00	13/03/2021 20:30	10
06/03/2022	NARPAT SINGH	65	M	2022/03/008668	82	166	1.66	29.75758656	UPPER MIDDLE CLASS		06/03/2022	10/03/2022 22:36	96
03/04/2022	Imrataram	47	M	2022/06/002072	85	170	1.7	29.41176471	UPPER MIDDLE CLASS	RURAL	3/4/22 22:00pm	03/04/2022 1:30am	4
06/03/2022	Khuman singh	65	M	2022/03/003744	56	156	1.56	23.01117686	LOWER MIDDLE CLASS	RURAL	6/3/22 6:00am	06/03/2022 14:45	8
17/07/2021	KARANDAS	58	M	2021/07/010026	60	176	1.76	19.36983471	LOWER CLASS	RURAL	17/07/2021 20:30	18/7/2021 1:00am	05:30
20/10/2021	MURALIDHAR	78	M	2021/10/019583	55	168	1.68	19.48696145	UPPER MIDDLE CLASS	URBAN	20/10/2021	20/10/2021 22:55	2
30/10/2021	HASTU DEVI	55	M	2021/10/019467	62	158	1.58	24.8357635	LOWER MIDDLE CLASS		30/10/2021 17:30pm	30/10/2021 22:30	6
20/11/2022	VIJAY SINGH	75	M	2021/11/010557	75	168	1.68	26.57312925	LOWER MIDDLE CLASS	URBAN	20/11/2021 9:30AM	20/11/2021 11:35PM	4
20/02/2022	PREMARAM	70	M	2022/02/011737	78	172	1.72	26.36560303	LOWER MIDDLE CLASS	RURAL	20/02/2022 07:00	20/2/2022 12.30pm	5.30hr
03/04/2021	RAM SWAROOP	25	M	2021/04/001110	58	162	1.62	22.10028959	UPPER MIDDLE CLASS	URBAN	3/4/2021 1.30pm	03/04/2021 22:00	9
21/11/2021	OM PRAKASH	72	M	2021/11/010743	76	176	1.76	24.53512397	UPPER CLASS	RURAL	21/11/2021 10:00am	21/11/2021 15:15	5
01/05/2021	KALAWATI DEVI	60	F	2021/05/001231	62	159	1.59	24.52434635	UPPER MIDDLE CLASS	URBAN	01/05/2021	03/05/2021 20:30	
15/07/2022	BHAGAVAN GIRI	60	M	2022/07/009587	58	162	1.62	22.10028959	LOWER MIDDLE CLASS	RURAL	15/7/22 5:00pm	15/07/2022 07:20	02:20
13/03/2022	KAMA RAM	48	M	2022/03/009392	84	170	1.7	29.06574394	LOWER CLASS	URBAN	13/3/2022 8:30pm	13/03/2022 10:30	2
23/03/2021	PARMILA KANWAR	55	F	2021/03/013468	63	156	1.56	25.88757396	UPPER MIDDLE CLASS	RURAL	23/3/2021 11:20pm	24/3/2021 7:00pm	8
05/04/2022	SADDIK KHAN	64	M	2022/03/018810	86	169	1.69	30.11099051	UPPER CLASS	URBAN	5/4/2022 6:30am	5/4/2022 9:00am	2.3
01/04/2022	SHARIF KHAN	23	M	2022/04/000129	68	162	1.62	25.91068435	UPPER MIDDLE CLASS	URBAN	1/4/2022 10:30am	1/4/2022 1:00pm	03:30
18/03/2022	DAKSHA DEVI	30	F	2022/03/003764	55	156	1.56	22.60026298	LOWER MIDDLE CLASS	RURAL	18/03/2022 04:00	18/03/2022 06:30	02:30
12/03/2022	NAVEEN KUMAR	67	M	2021/06/025369	62	154	1.54	26.14268848	LOWER CLASS	RURAL	12/03/2022 16:30	12/3/2022 22:00pm	06:30
16/07/2022	JAMNA DEVI	85	F	2022/07/010411	48	159	1.59	18.98659072	UPPER CLASS	URBAN	16/07/2022 04:00	16/07/2022	08:30
20/02/2022	HANUMAN LAL	74	M	2022/02/011871	86	159	1.59	34.01764171	UPPER MIDDLE CLASS	URBAN	20/2/2022 3:20pm	20/02/2022 16:30	1
13/10/2021	SURENDRA	40	M	2021/10/008225	80	168	1.68	28.3446712	LOWER CLASS	RURAL	13/10/2021 05:00	13/10/2021 10:30	05:30
01/05/2021	JEODEVI	80	F	2021/05/000071	65	158	1.58	26.03749399	UPPER CLASS	URBAN	01/05/2021 06:00	01/05/2021 10:30	4.3
18/11/2021	KANCHAN SINGHVI	74	F	2021/11/009146	68	159	1.59	26.89767019	UPPER MIDDLE CLASS	URBAN	18/11/2021 20:00	18/11/2021 23:30	3.3
16/11/2021	ASRAT KANWAR	70	F	2021/11/008309	56	158	1.58	22.43230252	UPPER MIDDLE CLASS	URBAN	16/11/2021 07:00	16/11/2021 11:30	04:30
15/07/2021	KAMLA	65	F	2021/07/009435	100	168	1.68	35.430839	LOWER MIDDLE CLASS	URBAN	15/07/2021 05:00	16/07/2021 12:00	7
04/05/2021	RAMESH	62	M	2021/05/001332	86	172	1.72	29.06976744	UPPER CLASS	URBAN	04/05/2021 17:00	04/05/2021 20:00	3
08/02/2022	DEVI LAL	65	M	2022/02/004849	75	168	1.68	26.57312925	UPPER MIDDLE CLASS	URBAN	08/02/2022 17:00	08/02/2022 22:45	05:45
01/04/2022	SUNIL	54	M	2022/04/000047	88	168	1.68	31.17913832	UPPER MIDDLE CLASS	URBAN	01/04/2022 07:00	01/04/2022 08:00	1
01/04/2022	OM PRAKASH SINGH	58	M	2022/02/002492	96	172	1.72	32.44997296	UPPER CLASS	URBAN	01/04/2022 19:00	01/04/2022 20:10	1
07/06/2022	PAPPAN SINGH	47	M	2022/07/002787	78	175	1.75	25.46938776	LOWER MIDDLE CLASS	URBAN	07/06/2022 10:30	7/6/2022 12:00pm	02:30
12/07/2022	SANTOSH KANWAR	22	F	2022/07/006958	69	165	1.65	25.34435262	LOWER CLASS	URBAN	12/07/2022	12/07/2022 19:30	01:30
23/07/2022	LAXMI SHARMA	72	F	2022/07/015843	48	158	1.58	19.22768787	UPPER CLASS	RURAL	23/07/2022 05:00	23/07/2022 10:30	05:30
25/07/2022	KISHORE KUMAR	24	M	2022/07/017779	69	162	1.62	26.29172382	UPPER MIDDLE CLASS	URBAN	25/07/2022 10:00	25/07/2022 04:00	10
19/07/2022	Mohan Lal	60	M	2022/07/011120	72	164	1.64	26.76977989	LOWER MIDDLE CLASS	URBAN	18/09/2022 14:00	18/09/2022 22:00	8
17/03/2022	SHANKAR LAL	70	M	2022/03/017650	88	172	1.72	29.74580855	UPPER MIDDLE CLASS	URBAN	17/03/22 8:00AM	17/03/22 10:30AM	01:30
29/07/2022	JITENDRA SINGH NIRWAN	73	M	2016/07/007391	92	163	1.63	34.62682073	UPPER CLASS	URBAN	19/09/2022 12:00	19/09/2022 08:00	7
01/02/2022	SOHNI	65	F	2022/02/000472	48	147	1.47	22.21296682	LOWER CLASS	RURAL	1/02/22 6:00AM	1/02/22 7:30AM	01:30
11/08/2022	LILA	40	F	2019/09/008525	46	159	1.59	18.19548277	LOWER MIDDLE CLASS	RURAL	11/08/2022 22:30	11/08/2022 01:00	3
12/02/2022	SHANKAR SINGH	76	M	2022/02/008893	79	172	1.72	26.70362358	LOWER CLASS	RURAL	12/02/22 6:00PM	12/02/22 8:15PM	02:15
07/02/2022	SARASWATI	55	F	2021/09/002427	56	159	1.59	22.15102251	UPPER MIDDLE CLASS	URBAN	07/02/22 1:30PM	07/02/22 4:00PM	02:30
16/07/2022	BHERARAM BISHNOI	26	M	2021/02/004181	54	169	1.69	18.90690102	UPPER CLASS	URBAN	10/07/2022 05:00	10/7/2022 12:000	7
21/02/2022	HIMTARAM	50	M	2022/02/012830	98	164	1.64	36.43664485	UPPER MIDDLE CLASS	URBAN	21/02/22 2PM	21/02/22 4:30PM	01:30
01/03/2022	SUJAN SINGH	75	M	2022/03/000361	65	172	1.72	21.97133586	UPPER MIDDLE CLASS	URBAN	1/3/22 11:00PM	1/3/22 2:00AM	04:00
16/08/2022	MANGI DEVI	34	F	2022/08/010681	64	159	1.59	25.31545429	UPPER MIDDLE CLASS		16/08/2022 15:30	16/08/2022 16:30	1
23/08/2022	KAILASH KANWAR	56	M	2022/08/015808	59	166	1.66	21.41094498	LOWER MIDDLE CLASS	RURAL	23/8/22 5:00 pm	23/08/2022 22:00	5
29/07/2022	RAKESH KOTHARI	50	M	2022/07/020200	52	160	1.6	20.3125	UPPER MIDDLE CLASS	URBAN	29/09/2022 10:00	29/09/2022 12:00	2
21/07/2022	ANDI DEVI	70	F	2022/07/016688	58	158	1.58	23.23345618	UPPER MIDDLE CLASS	URBAN	21/07/2022 07:00	21/07/2022 07:30	01:30
21/04/2022	BHOLA RAM	50	M	2022/04/013073	67	164	1.64	24.9107674	LOWER MIDDLE CLASS	URBAN	21/04/2022 05:00	21/04/2022 07:00	2
04/05/2022	PRATAPA RAM	73	M	2022/05/001906	73	174	1.74	24.11150746	UPPER CLASS	URBAN	04/05/2022 02:00	4/5/2022 4	2
03/07/2021	MANGILAL	72	M	2021/07/001507	82	178	1.78	25.88057064	UPPER MIDDLE CLASS	URBAN	03/07/2021 06:00	03/07/2021 08:45	03:45
04/05/2022	YOGESH DEVI	54	F	20217/09/000103	62	170	1.7	21.4532872	UPPER CLASS	URBAN	04/05/2022 02:00	4/5/20225	2
25/02/2022	RAKHI	40	F	2022/08/016716	56	168	1.68	19.84126984	LOWER MIDDLE CLASS	RURAL	25/08/2022 05:00	25/08/2022 06:30	01:30
30/04/2022	SURENDRA SINGH	93	M	2022/06/019365	85	175	1.75	27.75510204	UPPER MIDDLE CLASS	URBAN	30/04/2022 01:30	30/04/2022 04:00	03:30
11/03/2022	KARNARAM	48	M	2022/03/009392	92	168	1.68	32.59637188	LOWER MIDDLE CLASS	URBAN	11/03/2022	13/3/2022 10:00pm	36
14/04/2022	VASHUDEV	64	M	2021/05/000826	72	158	1.58	28.84153181	UPPER MIDDLE CLASS	RURAL	14/04/2022 05:30	14/4/2022 8:30	04:30
21/04/2022	BHOLA RAM	50	M	2022/04/013073	62	159	1.59	24.52434635	LOWER MIDDLE CLASS	RURAL	21/04/2022 20:10	22/04/2022 6:20am	08:30
06/07/2021	HULASI DEVI	76	F	2021/07/003212	56	161	1.61	21.60410478	UPPER CLASS	RURAL	6/7/2021 7:00am	06/07/2021 17:00	10
16/06/2021	CHUTAR SINGH	62	M	2021/06/010651	68	174	1.74	22.46003435	LOWER MIDDLE CLASS	RURAL	16/6/2021 7:00am	16/06/2021 09:30	02:30
08/06/2021	BHUNDA RAM	58	M	2021/06/007769	58	169	1.69	20.30741221	UPPER MIDDLE CLASS	URBAN	08/09/2021 08:00	010/06/2021 05:50:00	36
07/06/2021	BAKWAR SINGH	66	M	2021/06/002430	68	163	1.63	25.59373706	UPPER MIDDLE CLASS	URBAN	07/09/2021 08:00	07/06/2021 11:00	3
16/06/2021	KANKAR DEVI	24	F	2021/06/006759	68	163	1.63	25.59373706	LOWER CLASS	RURAL	16/09/2021 07:00	16/06/2021 12:00	5
23/03/2022	RAGHU NATH	42	M	20222/03/001416	88	169	1.69	30.8112461	UPPER CLASS	URBAN	23/3/2022 10	23/03/2022	01:30
20/11/2021	KHETARAM	75	M	2021/11/010605	80	168	1.68	28.3446712	LOWER MIDDLE CLASS	RURAL	20/11/2021 10:00	20/11/2021 04:00	6
19/03/2022	RAGHU NATH RAM	76	M	2022/01/030204	74	175	1.75	24.16326531	LOWER MIDDLE CLASS	URBAN	19/03/2022 11:35	19/03/2022 06:00	7
06/01/2022	SAWAI CHAND CHITAR	55	M	2022/01/023224	78	162	1.62	29.7210791	UPPER MIDDLE CLASS	RURAL	06/01/2022 05:00	06/01/2022 06:30	01:30
02/01/2022	MAHIPAL SINGH CHAMPAWAT	55	M	2022/01/019841	69	158	1.58	27.63980131	UPPER MIDDLE CLASS	URBAN	01/02/2022 05:00	01/02/2022 06:20	1
04/01/2022	ARJUN SINGH	56	M	2022/01/022561	86	178	1.78	27.1430375	LOWER MIDDLE CLASS	RURAL	04/01/2022 11:30	05/01/2022 12:45	24
12/01/2022	SHYAMLAL	80	M	2022/01/026576	67	164	1.64	24.9107674	UPPER CLASS	URBAN	12/01/2022 05:00	12/01/00022 6:0	01:30
24/07/2021	SHIVDAYAL	59	M	2022/05/007807	72	169	1.69	25.20920136	LOWER MIDDLE CLASS	URBAN	24/09/2021 08:00	24/09/2021 10:30	02:30
04/07/2022	VIJAY VERMA	35	M	2022/06/003210	56	162	1.62	21.33821064	UPPER MIDDLE CLASS	RURAL	05/09/2022 02:30	05/06/2022 08:30	03:30
06/06/2021	NIKHIL	36	M	2021/06/002033	92	176	1.76	29.70041322	UPPER CLASS	URBAN	06/09/2021 04:30	06/06/2021 06:00	02:30
23/01/2021	GOPI	76	F	2022/01/032063	49	164	1.64	18.21832243	UPPER CLASS	RURAL	23/01/2021 04:30	24/01/2022	24
23/01/2022	MANOHAR KUMAR RANKA	58	M	2022/01/032143	72	173	1.73	24.05693475	LOWER CLASS	URBAN	23/01/2022 05:30	23/01/2022 10:30	05:30
24/01/2022	BHAGIRATH	62	M	2022/01/032691	62	163	1.63	23.33546614	LOWER MIDDLE CLASS	URBAN	24/01/2022 14:00	24/01/2022 17:00	02:30
28/12/2021	SUKHARAM	45	M	2021/12/017111	76	168	1.68	26.92743764	UPPER CLASS	RURAL	28/12/2021 12:00	28/12/2021 03:45	01:30
30/12/2021	PARBHU RAM	50	M	2021/12/018800	63	172	1.72	21.29529475	LOWER MIDDLE CLASS	URBAN	30/12/2021 11:00	30/12/2021 01:00	02:00
24/07/2022	MOHAN PYARI VYAS	87	F	2022/07/016873	52	149	1.49	23.42236836	UPPER MIDDLE CLASS	URBAN	25/07/2022 04:00	25/07/2022 05:30	00:45
01/07/2022	BARJU	75	F	2022/07/000147	49	153	1.53	20.93212012	UPPER MIDDLE CLASS	RURAL	1/8/2022 8	01/08/2022	02:00
30/07/2022	JEEVAN SINGH	75	M	2022/07/021085	69	163	1.63	25.97011555	LOWER MIDDLE CLASS	URBAN	30/07/2022 05:00	30/07/2022 07:30	02:30
16/06/2022	JAGRAM	80	M	2022/06/011913	87	175	1.75	28.40816327	UPPER CLASS	RURAL	15/06/2022 05:00	16/06/2022 10:00	12
18/07/2021	HARIRAM	32	M	2022/06/013664	70	168	1.68	24.8015873	LOWER MIDDLE CLASS		18/07/2021 04:00	18/07/2022 10:00	00:00
18/07/2022	OM PRAKASH	70	M	2022/06/015569	58	172	1.72	19.605192	UPPER MIDDLE CLASS	RURAL	20/06/2022 05:00	20/06/2022 06:20	01:20
25/06/2022	MOHANI	68	F	2022/06/019381	62	160	1.6	24.21875	LOWER MIDDLE CLASS	RURAL	25/06/2022 12:30	25/06/2022 03:30	04:30
05/07/2022	PUKHRAJ	40	M	2022/07/000699	69	174	1.74	22.79032897	UPPER MIDDLE CLASS	URBAN	05/07/2022 12:00	06/07/2022 06:00	36:00:00
06/07/2022	ANWAR	71	M	2022/07/001152	56	159	1.59	22.15102251	UPPER MIDDLE CLASS	RURAL	02/07/2022 10:00	03/07/2022 03:00	14:00
28/07/2022	GHANSHYAM	28	M	2022/07/019818	68	174	1.74	22.46003435	LOWER MIDDLE CLASS	URBAN	28/07/2022 11:00	28/07/2022 03:00	06:00
10/01/2022	DHANNA RAM	65	M	2022/01/024226	87	169	1.69	30.46111831	UPPER MIDDLE CLASS	URBAN	08/01/2022 10:30	10/01/2022 09:30	36:00:00
13/01/2022	SATYA PRAKASH	60	M	2022/01/027799	66	168	1.68	23.38435374	UPPER MIDDLE CLASS	RURAL	13/01/2022 14:30	13/01/2022 16:30	02:30
16/01/2022	MANGLA RAM	60	M	2022/01/028319	56	159	1.59	22.15102251	LOWER CLASS	RURAL	16/01/2022 17:00	16/01/2022 21:00	04:00
20/08/2022	SAKUNTALA	82	F	2022/08/012653	68	155	1.55	28.30385016	UPPER MIDDLE CLASS	RURAL	20/08/2022 05:00	20/08/2022	04:00
07/07/2022	HEERI DEVI	60	F	2022/07/005109	76	164	1.64	28.25698989	LOWER MIDDLE CLASS	URBAN	07/08/2022 01:30	28/02/2022 04:00	05:30
19/07/2022	SHYAMAWATI	55	F	2022/08/012674	68	164	1.64	25.2825689	UPPER MIDDLE CLASS	RURAL	19/08/2022 17:30	19/08/2022 20:30	03:30
16/08/2022	YUSUF	69	M	2022/08/012674	84	166	1.66	30.4833793	UPPER MIDDLE CLASS	URBAN	16/08/2022 02:00	16/08/2022 05:30	03:30
10/08/2022	AMRA RAM	61	M	2022/08/006786	65	168	1.68	23.03004535	LOWER MIDDLE CLASS	RURAL	10/08/2022 04:30	10/08/2022 07:00	03:30
09/08/2022	NATHU RAM	60	M	2022/08/006238	76	172	1.72	25.68956193	UPPER CLASS	URBAN	08/08/2022 01:00	08/08/2022 02:30	02:30
03/08/2022	ARAB KHAN	65	M	2017/01/022318	62	159	1.59	24.52434635	LOWER MIDDLE CLASS	URBAN	03/08/2022 15:30	03/08/2022 16:30	01:00
03/08/2022	KANHAIYA LAL	68	M	2022/08/001974	78	162	1.62	29.7210791	UPPER CLASS	URBAN	02/08/2022 22:00	03/08/2022 07:00	08:00
30/04/2022	GODAVARI	72	M	2022/04/019400	56	164	1.64	20.82093992	LOWER MIDDLE CLASS	URBAN	02/08/2022 14:00	02/08/2022 17:30	03:30
01/05/2022	PARIMAL SUNDAR CHOUDARY	83	M	2019/06/001320	68	162	1.62	25.91068435	UPPER CLASS	RURAL	06/05/2022 07:00	06/05/2022 08:00	00:45
11/05/2022	SANGEETA	58	F	2022/05/006252	84	168	1.68	29.76190476	UPPER MIDDLE CLASS	URBAN	11/05/2022 04:45	11/05/2022 12:45	10:00
24/05/2022	GODHARAM	30	M	2022/05/015445	68	162	1.62	25.91068435	UPPER CLASS	URBAN	24/05/2022 04:00	24/05/2022 14:00	08:00
06/06/2022	VIJAY VERMA	35	M	2022/06/003210	75	178	1.78	23.67125363	LOWER MIDDLE CLASS	URBAN	24/05/2022 04:00	25/05/2022 14:00	28:00:00
13/06/2022	PRAKASH KANWAR	65	M	2022/06/009727	76	166	1.66	27.58020032	UPPER MIDDLE CLASS	RURAL	13/06/2022 05:40	13/06/2022 09:00	05:45
18/04/2022	PURVA	22	F	2022/04/010358	65	168	1.68	23.03004535	LOWER CLASS	URBAN	18/4/22 7:00AM	18/4/22 8:00AM	1
04/10/2022	VIJAY MEHTA	56	M	2015/1/009055	56	169	1.69	19.60715661	UPPER MIDDLE CLASS	URBAN	10/4/22 8:00PM	10/4/22 11:00PM	3
14/08/2022	ASHOK	58	M	2022/08/009080	65	168	1.68	23.03004535	LOWER MIDDLE CLASS	RURAL	14/08/2022 10:00	15/08/2022 15:30	12:00
27/08/2022	DHEERAJ	30	M	2022/08/018465	72	176	1.76	23.24380165	LOWER MIDDLE CLASS	URBAN	25/08/2022 14:00	27/08/2022	48:00:00
27/08/2022	HEMALATHA	65	F	2022/08/018931	59	156	1.56	24.24391847	UPPER CLASS	URBAN	25/08/2022 17:00	25/08/2022 19:30	04:00
29/08/2022	SURJARAM	62	M	2022/08/019528	76	162	1.62	28.95900015	UPPER MIDDLE CLASS	URBAN	28/08/2022 05:00	29/08/2022	36:00:00
23/08/2022	ABALRAFI	53	M	2022/10/000869	58	168	1.68	20.54988662	UPPER MIDDLE CLASS	URBAN	03/08/2022 10:00	04/08/2022 08:00	12:00:00
07/11/2021	KALAWATI DEVI	60	F	2021/05/001231	55	159	1.59	21.75546853	LOWER MIDDLE CLASS	RURAL	07/11/2021 08:00	07/11/2021	04:00
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