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# Independent Predictors of Functional Outcome of Acute Stroke among Population of Southern Coastal India - A Hospital Based Prospective Longitudinal Study

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**Abstract:** ***Introduction: Stroke is the disease of the cerebral blood vessels nourishing the brain. Strokes represent one of the major causes of mortality, functional dependency, and long-term disability in adults. Objective: To determine the parameters predicting the functional outcome at 3 months in acute stroke patients. Materials and Methods: It was a prospective longitudinal study done at Department of Neurology, Narayana Medical college from December 2018 to May 2020. Patients who presented with acute stroke to the Neurology OPD & Emergency Departments were included in the study. Various epidemiological, clinical and investigatory (lab & imaging) variables were studied. All the patients were followed for 3 months after discharge. The functional outcome at 3 months was analysed with reference to all the mentioned variables. Results: Out of the 653 patients, 348 patients (53.29%) were followed up for 3months and analysed. There was a significant difference between patients who had good and poor functional outcome at 3 months as assessed by modified rankin scale (mRS) score with respect to demographic data including age, education, employment and economic state, awareness of vascular risk factors, risk factors including Stroke in young, hypertension, diabetes mellitus, symptom timeline including delay at presentation of more than 4.5 hours, mode of transport to registry hospital, time duration between last known normal to hospital arrival and time duration from ictus to first medical contact, with respect to symptoms at presentation including headache and blurring of vision, examination findings including respiratory rate, Glasgow Coma Scale(GCS) at admission, higher mental function at admission and National Institute of Health stroke scale(NIHSS)score at admission, complications like aspiration pneumonia sepsis and bed sore, time duration for first consult of stroke specialist and duration of hospital stay and with respect to investigations including total count, Neutrophil to lymphocyte ratio, low density lipoprotein cholesterol (LDL) and creatinine. Conclusion: This study observed that high economic state was independently associated with good functional outcome while older age and prolonged duration of history of hypertension, severe grade of GCS at admission, moderate grade of NIHSS score at admission and prolonged duration of hospitalization were found to be independently associated with poor functional outcome.***

**Keywords:** stroke, predictors, functional outcome, mRS

## 1. Introduction

Stroke as a syndrome is the leading cause of disability in the world, less is known about the independent factors that influence stroke outcomes. Predicting functional outcome in stroke is challenging to most clinicians, partly because of the complexity of the condition and also because of the lack of validated prognostic models.

Accurate prediction of functional outcome in patients with stroke has the potential to enhance clinical care as well as improve the quality of stroke research. It can also facilitate education and counselling of patients and families, and streamline planning for acute stroke management and post stroke rehabilitation.

The use of formal prognostic models to predict functional outcome have not been used in clinical stroke rehabilitation because large representative cohorts have not been studied and existing models are not well validated[1].Patients experiencing deficits as a result of a stroke are worried about their expected outcome. Identifying predictors of functional outcome may be of assistance to physicians when confronted with these concerns from stroke patients.

Improvement in the estimation of clinical outcomes could result in more specific management of stroke rehabilitation as well as clearer informing of patients and their care givers. While the mortality associated with stroke has decreased, the morbidity associated with the disease remains high, with a huge cost burden.

The present study was designed to study the epidemiological, clinical, laboratory and radiologic factors that are associated with poor functional outcome in patients who presented with acute stroke.

## 2. Materials and Methods

The prospective longitudinal study was done at Department of Neurology from December 2018 to May 2020. The study was approved by Institute ethics committee.

(30/NMCIEC/2018). A convenience sampling method was followed.

The study was done on 348 patients with acute stroke (both

out patients and in patients). A proforma was prepared which included detailed history, clinical examination, details of in hospital management and requisite investigations done at our hospital. History was noted from the patient, or by standers (if the patient was unable to interact due to the illness per se) included the demographic data, medical history, awareness of the risk factors, and management details of stroke and the symptoms time line. Complications like recurrent stroke, aspiration pneumonia, seizure, bedsore, sepsis were noted. The patients were followed up to discharge and 3 months subsequently. A detailed clinical examination was done and neurological deficits were identified. Relevant investigations were done including laboratory (CBP, RFT, serum electrolytes, fasting lipid profile, HbA1C) and brain imaging was done to identify the underlying pathophysiological mechanism and etiology. The stroke functional outcome at 3 months was assessed using the modified Rankin scale (mRS) score.

**Grading of mRS[2]**

- 0-2- Good functional outcome
- 3-6–Poor functional outcome

**Statistical Analysis**

The data values were entered into MS–Excel and statistical analysis has been done by using IBMSPSS Version 25.0. For categorical variables the values are represented as number and percentages. To test association between the groups, chi-square test has been used. For continuous variables, the values are represented as mean and standard deviation. To test the mean difference between three or more groups, ANOVA (Analysis of Variance) test with *post hoc* (Tukey's) test has been used. All the p values less than 0.05 are considered as statistically significant. Multivariate analysis has been done using logistic regression technique to identify the independent predictors among the studied variables for severity of stroke at admission and also for functional outcome after 3 months.

## 3. Results

A total number of 653 acute stroke patients were enrolled, out of which, only 348 patients (53%) (Sample number) were followed up for three months and analyzed to identify predictors for functional outcome.

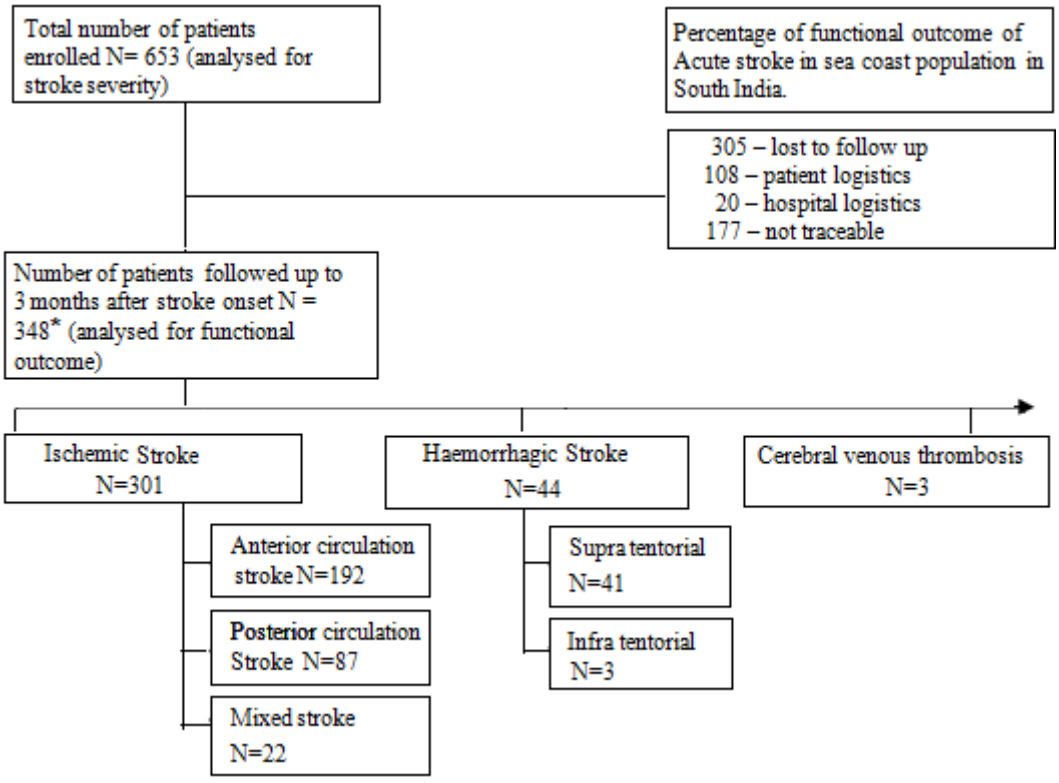


**Figure1:** Study sample distribution

Of the 348 patients, 201 patients (58%) had good functional outcome and the remaining 147 (42%) had a poor functional outcome. Among the 305 patients who could not be followed up, 108 patients (35%) had their own logistic reasons, 20 (7%) had hospital logistic reasons for not following up, and the remaining 177 (58%) could not be traced (invalid details).

104 independent variables including epidemiological, clinical and investigatory parameters were tested against functional outcome at three months by univariate analysis.

Epidemiological variables included were age, stroke in young, sex, residence, education, marital status, employment, religion, economic state, awareness of vascular risk factors, stroke/ coronary artery disease (CAD), thrombolytics, antiplatelets, physiotherapy, speech therapy, botox therapy, and past history of risk factors for stroke like prior history of stroke, CAD, transient ischemic attack (TIA), other cardiovascular risk factors, family history of stroke/CAD, history of obesity, chronic kidney disease (CKD), dyslipidemia, hypertension, diabetes, migraine, hormone replacement therapy, alcohol intake, smoking and

symptoms timeline including details of month and season wise incidence of stroke, time of onset, time of arrival to hospital, time of admission, duration between last known normal to symptom onset, duration between last known normal to hospital arrival, duration from ictus to first medical contact and basic admission details including first evaluated area, ambulatory status at ictus, delay of more than 4.5 hours (door to needle time), first contact with medical professional, mode of transport to first medical professional, mode of transport to registry hospital.

**Table 1:** Univariate analysis of epidemiological factors (categorical variables) with statistical significance for functional outcome

| Variables | Outcomes of 348(100%) PATIENT (based on mRS at 3 months) | | Total (n%) | $X^2$- Value | p-Value |
|---|---|---|---|---|---|
| | Poor Functional Outcome (n%)147(42%) | Good Functional Outcome (n%)201(58%) | | | |
| **Education** | | | | | |
| Primary | 24(16%) | 68(34%) | 26.4 | 54.946 | .000 |
| Secondary | 6(4%) | 42(21%) | 13.8 | | |
| Tertiary | 0(0%) | 8(4%) | 2.3 | | |
| Nil | 114(78%) | 80(40%) | 55.7 | | |
| Unknown | 3(2%) | 3(1%) | 1.7 | | |
| **Employment** | | | | | |
| Professional | 0 | 2(1%) | 0.6 | 17.631 | 0.014 |
| Trained | 6(4%) | 17(9%) | 6.6 | | |
| Skilled | 25(17%) | 30(15%) | 15.8 | | |
| Semi-skilled | 17(12%) | 29(14%) | 13.2 | | |
| Unskilled | 15(10%) | 34(17%) | 14.1 | | |
| Housewife | 52(35%) | 39(19%) | 26.1 | | |
| Unemployed | 28(19%) | 38(19%) | 19 | | |
| Retired | 4(3%) | 12(6%) | 4.6 | | |
| | | | | | |
| **Economic status (income per month in rupees)** | | | | | |
| 7533 and above | 10(7%) | 46(23%) | 16.1 | 90.496 | .000 |
| 3766-7532 | 16(11%) | 74(37%) | 25.9 | | |
| 2260-3765 | 5(3%) | 21(10%) | 7.5 | | |
| 1130-2259 | 6(4%) | 12(6%) | 5.2 | | |
| 1129 and below | 110(75%) | 48(24%) | 45.4 | | |
| **Awareness of vascular** | | | | | |
| **Rick factors** | 111(76%) | 113(56%) | 64.4 | 13.777 | .000 |
| Unknown | 36(24%) | 88(44%) | 35.8 | | |
| Known | | | | | |
| **Stroke in young** | | | | | |
| Yes | 4(3%) | 20(10%) | 6.9 | 6.911 | 0.009 |
| No | 143(97%) | 181(90%) | 93.1 | | |
| **Hypertension** | | | | | |
| >1year | 88.0(60%) | 55(27%) | 41.1 | 43.342 | .000 |
| <1year | 13(9%) | 12(6%) | 7.2 | | |
| Unknown | 1.0(1%) | 3(2%) | 1.1 | | |
| No | 45(30%) | 131(65%) | 50.6 | | |
| **Diabetes** | | | | | |
| >1year | 70(48%) | 59(29%) | 37.1 | 12.171 | 0.007 |
| <1year | 7(5%) | 12(6%) | 5.5 | | |
| Unknown | 1.02(1%) | 2(1%) | 0.9 | | |
| No | 69(46%) | 128(64%) | 56.6 | | |
| **>4.5 hours delay(door To needle time)** | | | | | |
| Yes | 94(64%) | 88(44%) | 52.3 | 13.838 | .000 |
| No | 53(36%) | 113(56%) | 47.7 | | |
| **Mode of transport to registry hospital** | | | | | |
| Ambulance | 21(14%) | 30(15%) | 14.7 | 40.712 | .000 |
| Private | 75(51%) | 144(72%) | 629 | | |
| Private and public | 0 | 7(3%) | 2 | | |
| Public | 51(35%) | 18(9%) | 19.8 | | |
| Other | 0 | 2(1%) | 0.6 | | |

*<0.05significant ‘p’value, mRS modified Rankin scale

**Table 2:** Univariate analysis of epidemiological parameters (continuous variables) with statistical significance -for functional outcome

| Variables | Total (N) | Mean | Standard Deviation | t-Value/ f-Value | p-Value |
|---|---|---|---|---|---|
| **Age[years]** | | | | | |
| Poor functional outcome | 147 | 70.33 | 8.261 | 8.880/12.948 | .000 |
| Good functional outcome | 201 | 56.65 | 10.685 | | |
| **Duration between last known normal to hospital arrival [hours]** | | | | | |
| Poor functional outcome | 147 | 67.7816 | 67.71659 | 7.183/ 3.922 | .000* |
| Good functional outcome | 201 | 39.5786 | 65.17244 | | |
| **Duration from ictus to first medical contact [hours]** | | | | | |
| Poor functional outcome | 147 | 23.3546 | 29.90463 | 4.014/ 2.871 | .004* |
| Good functional outcome | 201 | 14.1535 | 29.25101 | | |

*<0.05 significant 'p' value

As illustrated in table 1&2, there was a significant difference between patients who had good and poor functional outcome at 3 months as assessed by mRS score (tables 1 and 2) with respect to demographic data including age, education, employment and economic state, awareness of vascular risk factors, risk factors including Stroke in young, hypertension, diabetes mellitus, symptom timeline including delay at presentation more than 4.5 hours (door to needle time), mode of transport to registry hospital, time duration between last known normal to hospital arrival and time duration from ictus to first medical contact.

Clinical profile composed of symptoms at admission including headache, vomiting, giddiness, double vision, blurring of vision, weakness, altered level of consciousness, seizures, difficulty in speech, difficulty in swallowing , drooping of upper eyelid, deviation of mouth, unsteadiness of gait, tingling and parasthesias, pain over half of the body, dysphagia, hoarseness of voice, symptoms evolution and examination finding sat admission including pallor, blood pressure, heart rate, temperature, respiratory rate, Glasgow Coma Scale (GCS) grading, National Institute of Health Stroke Scale (NIHSS) score at admission, higher mental functions, dysarthria, aphasia, sensory abnormalities, cerebellar system abnormalities, abnormal gait and in hospital management details including duration from arrival to nurse visit (in minutes), duration from arrival to stroke specialist consult (in hours), duration of hospital stay (in days), swallow assessment duration from arrival (in hours) and complications including recurrent stroke, cardiogenic shock, aspiration pneumonia, sepsis, bedsore. Investigatory profile include carotid Doppler, 2D echo cardiography, blood sugars at admission, haemoglobin, total leukocyte count, platelet count, Neutrophil to Lymphocyte ratio (NL ratio), total cholesterol, triglycerides, high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), creatinine, serum sodium, potassium, random glucose, fasting glucose, post prandial glucose and Glycosylated hemoglobin (HbA1C).

**Table 3:** Univariate analysis of clinico-investigatory parameters (categorical variables) with statistical significance for functional outcome

| Variables | Outcomes (based on mRs at 3 months) | | Total (n%) | $X^2$- Value | P- Value |
|---|---|---|---|---|---|
| | Poor Functional Outcome (n%) 147 (42%) | Good Functional Outcome (n%) 201 (58%) | | | |
| **Headache** | | | | | |
| Present | 30(20%) | 21(10%) | 14.7 | 6.735 | **0.009** |
| Absent | 117(80%) | 180(90%) | 85.3 | | |
| **Blurring of vision** | | | | | |
| Present | 86(18%) | 21(10%) | 13.8 | 4.479 | **0.034** |
| Absent | 61(82%) | 180(90%) | 86.2 | | |
| **Respiratory** | | | | | |
| Abnormal | 54(59%) | 83(41%) | 48.6 | 10.067 | **0.002** |
| Normal | 37(41%) | 118(59%) | 51.4 | | |
| **GCS grading at admission** | | | | | |
| Severe | 54(37%) | 4(2%) | 16.7 | 93.956 | **.000** |
| Moderate | 37(25%) | 29(14%) | 19 | | |
| Mild | 56(38%) | 168(84%) | 64.4 | | |
| **NIHSS at admission** | | | | | |
| Severe | 62(42%) | 1(1%) | 18.1 | 138.535 | **.000** |
| Moderate-severe | 16(11%) | 10(5%) | 7.5 | | |
| Moderate | 65(44%) | 105(52%) | 48.9 | | |
| Mild | 4(3%) | 85(42%) | 57.8 | | |
| **Higher mental functions** | | | | | |
| Abnormal | 83(57%) | 44(22%) | 36.5 | 43.787 | **.000** |
| Normal | 64(43%) | 157(78%) | 63.5 | | |
| **Aspiration pneumonia** | | | | | |
| Present | 67(46%) | 0(0%) | 19.3 | 113.456 | **.000** |
| Absent | 80(54%) | 201(100%) | 80.7 | | |
| **Sepsis** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Present | 40(27%) | 0(0%) | 11.5 | 61.797 | **.000** |
| Absent | 107(73%) | 201(100%) | 88.5 | | |
| **Bedsore** | | | | | |
| Present | 10(7%) | 0(0%) | 2.9 | 14.078 | **.000** |
| Absent | 137(93%) | 201(100%) | 97.1 | | |
| **Total leukocyte count** | | | | | |
| Abnormal | 68(46%) | 53(26%) | 34.8 | 14.81 | **.000** |
| Normal | 79(54%) | 148(74%) | 65.2 | | |
| **NL ratio** | | | | | |
| >=5.90 | 54(37%) | 30(15%) | 24.1 | 22.082 | **.000** |
| 3.21-5.89 | 38(26%) | 68(34%) | 30.5 | | |
| <=3.20 | 55(37%) | 103(51%) | 45.4 | | |
| **LDL** | | | | | |
| Abnormal | 52(35%) | 43(21%) | 27.3 | 8.362 | **0.004** |
| Normal | 95(65%) | 158(79%) | 72.7 | | |
| **Creatinine** | | | | | |
| Abnormal | 58(39%) | 37(18%) | 27.3 | 18.952 | **.000** |
| Normal | 89(61%) | 164(82%) | 72.7 | | |

*<0.05 significant 'p' value, GCS Glasgow Coma Scale, LDL low density lipoprotein cholesterol, mRS Modified Rankin scale, NIHSS National Institute of Health Stroke Scale, NL ratio neutrophil to lymphocyte ratio.

**Table 4:** Univariate analysis of clinical parameters (continuous variables) with statistical significance for functional outcome

| Variables | Total (N) | Mean | Standard Deviation | t-Value/ f-Value | P-Value |
|---|---|---|---|---|---|
| Duration from arrival to Stroke specialist consult [hours] | | | | 7.582/ 2.395 | .017* |
| Poor functional outcome | 147 | 4.5603 | 7.38698 | | |
| Good functional outcome | 201 | 3.0223 | 4.55236 | | |
| Duration of hospital stay [days] | | | | 272.295/ 9.463 | .000* |
| Poor functional outcome | 147 | 10.5816 | 5.91349 | | |
| Good functional outcome | 201 | 6.199 | 2.44544 | | |

*<0.05significant'p'value

As illustrated in table 3&4, there was significant difference between patients who had good and poor functional outcome at 3 months assessed by MRS score with respect to symptoms at presentation including headache and blurring of vision, examination findings including respiratory rate, GCS at admission, higher mental function sat admission and NIHSS score at admission, complications like aspiration pneumonia, sepsis and bed sore, time duration for first consult of stroke specialist and duration of hospital stay.

There was a significant difference between participants who had good and poor functional outcome at three months assessed by mRS score with respect to total leukocyte count, NL ratio, LDL and creatinine.

**Table 5:** Multi variate analysis of all significant variables for functional outcome with statistical significance

| Variable | B | STD. ERROR | WALD | SIG. | EXP(B) | 95% Confidence Interval for Exp (B) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower Bound | Upper Bound |
| Age | -0.507 | 0.219 | 7.703 | **0.006** | 0.602 | 0.392 | 0.926 |
| Economic state (upper) | 10.251 | 4.679 | 4.8 | **0.028** | 23.61 | 2.945 | 27.743 |
| Hypertension (>1year) | -7.499 | 2.951 | 6.455 | **0.011** | 0.001 | 0 | 0.18 |
| Hypertension (<1year) | -8.763 | 3.838 | 5.213 | **0.022** | 0 | 0 | 0.289 |
| GCS grading at admission | -8.341 | 4.153 | 4.034 | **0.045** | 0 | 0 | 0.817 |
| NIHSS at admission | -6.333 | 3.18 | 3.965 | **0.046** | 0.002 | 0 | 0.905 |
| Length of stay (in days) | -0.428 | 0.178 | 5.801 | **0.016** | 0.652 | 0.461 | 0.923 |

*<0.05significant'p'value, GCS (Glasgow Coma Scale, ) NIHSS (National Institute of Health Stroke Scale)

As illustrated in table 5, older age, hypertension, severe grading of GCS, moderate grade of NIHSS and prolonged duration of hospital stay were independent predictors of poor functional outcome at three months. Upper and upper-middle-class (high economic state) were found to be independent predictors of good functional outcome.

## 4. Discussion

The present study is a prospective longitudinal study conducted in a tertiary care teaching hospital. In the present study, all the patients with acute stroke, who satisfied all the inclusion and exclusion criteria, admitted in the department of Neurology were enrolled and managed according to the guidelines and were analyzed to identify the predictive factors for functional outcome based on the mRS score at follow up after three months respectively. In multi variate analysis, old age, history of systemic hypertension of duration more than one year, low GCS, NIHSS score more than 5, and a prolonged hospital stay were independent predictors of poor functional outcome at three months. Good socioeconomic state was an independent predictor for good functional outcome.

Older age was independently associated with poor functional outcome after 3months of follow-up, which is well established in many studies. In Hanen Ghazali. etal.[3], age more than 70 years was independently associated with

poor functional outcome. In Appelros et al.[4], age was confirmed as a risk factor for mortality and dependency with in the first year after a first- ever stroke. In a Korean study[5]published in 2016, advanced age was identified as a predictive factor of severe functional disability in univariate analysis six months after episode. Damak. et al.[6]also identified the same at one month follow-up.

Linfante I. et al.[7], an American study published in 2015, identified age of more than 80 years as an independent predictive factor of poor 90-day outcome in multivariate analysis. In YH Wang et al.[8], it was indicated that based on age, the potential for motor function improvement at three months post-stroke can be predicted.

Severe grading of GCS was independently associated with poor functional outcome after three months of follow-up. This may implicate that the depth of coma, a measure of neurological impact of the disease, has a greater influence

on the functional outcome. In Fanshawe Metal.[9], GCS<10 during assessment was associated with increased mortality and poor functional outcome. In Hanen Ghazali.et al.[3], GCS <11 was independently associated with poor functional outcome. Baird AE et al.[10]showed that the mortality rate in ischemic stroke is 90%; if GCS level ≤8.In Khadija Sonda Moalla et al.[11], low GCS was found as a poor prognostic factor for stroke after one month of follow-up. In a Korean study[5] published in 2016, low GCS was identified as a predictive factor of severe functional disability in univariate analysis at six months after episode.

History of hypertension for more than one year was independently associated with poor functional outcome at three months. Hypertensive disorders promote stroke through increased shear stress, endothelial dysfunction, and large artery stiffness that transmits pulsatile flow to the cerebral micro circulation.

Hypertension also promotes cerebral small vessel disease through several mechanisms, including hypo perfusion, diminished auto regulatory capacity and localized increase in blood-brain barrier permeability. In hypertension, the cerebral blood flow auto regulatory curve is shifted to higher pressures, making the patient susceptible to hypotensive brain injury. Patients with pre-existing hypertension have small amounts of salvageable tissue (penumbra) and larger infarctions than normotensive patients, although lower blood pressure is also detrimental in stroke[12]. In Leonardi-Bee, J etal.[12], high blood pressure and low blood pressure were independent prognostic factors for poor outcome.

NIHSS score >5 [moderate grade] was independently associated with poor functional outcome on multivariate regression analysis. Severe and moderate to severe grades of NIHSS were also associated with poor functional outcome but have not attained statistical significance, probably owing low sample size in these groups of patients. In Hanen Ghazali. et al.[3], NIHSS > 11 was independently associated with poor functional outcome. In a Korean study[5] published in 2016, high NIHSS was identified as a predictive factor of severe functional disability in univariate analysis at six months after episode. Linfante I., et al.[7], an American study published in 2015, identified in multivariate analysis NIHSS score ≥ 18 as an independent predictive factor of poor 90-day outcome. In Khadija Sonda Moalla et al.[11]high NIHSS was a poor prognostic factor for stroke after one month of follow-up.

Prolonged length of stay in hospital was independently associated with poor functional outcome. The length of the hospital stay may represent the severity of medical complications after stroke onset. Hence the prevention and reduction of medical complications should be the goal in hospitalized patients, thereby reducing the duration of hospital stay for a good functional outcome. In a Korean study[5] published in 2016, long duration of hospitalization was identified as a predictive factor of severe functional disability in univariate analysis at six months after episode.

Socioeconomic status comprising upper and upper-middle class was independently associated with good functional outcome. Socioeconomic status has been associated with inequalities in the delivery of care across the stroke pathway. In a US cohort study[13], patients of higher socioeconomic status were more likely to receive post-acute stroke rehabilitation. In a Danish nationwide study, compared with high-income patients, low-income patients were less likely to receive seven specific care processes (including stroke unit care, scan, anti-platelets or anticoagulation, assessment by a physiotherapist or occupational therapy) after stroke[14]. In Rey V et al.[15], private insurance status has previously been shown to predict favourable outcome in stroke patients up to three months after stroke, which probably is indicative of a higher socioeconomic status.

## 5. Conclusion

Stroke remains an important cause of disability and death worldwide. Due to expanding population numbers and ageing as well as the increased prevalence of modifiable risk factors the burden of stroke has increased substantially over the past few decades globally, especially in low and middle income countries. To determine the predictors is of paramount importance for clinicians to identify patients who are at higher risk for more severe strokes and death. High economic state [upper and upper middle class] was found to be independently associated with good functionaloutcomeduring3 months follow up. Epidemiological variables including older age and duration of history of hypertension and clinical parameters including severe grade of GCS at admission, moderate grade of NIHSS score at admission and prolonged duration of hospitalization were associated with poor functional outcome after 3 months follow up.

**Conflicts of interest:** None

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