

# Prevalence and Associated Factors of Psychological Distress of Patients with Stroke Attending a Neurology Clinic – An Analytical Cross-sectional Study

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# **Abstract**

**Background**: A vast range of factors lead to psychological distress among stroke patients, causing poor outcomes. This study aimed to assess the prevalence of psychological distress and identify the associated factors among stroke patients attending the Neurology Clinics of the National Hospital of Sri Lanka (NHSL), Colombo. **Methods**: A descriptive cross-sectional study with an analytical component was conducted among 177 patients with stroke attending the Neurology Clinics of the NHSL, Colombo, who were sampled by multistage random sampling. Psychological distress was assessed using the Kessler Psychological Distress Scale (K-10). Data collected under 6 domains underwent initial bivariate analysis using Chi-square and Fisher's Exact Tests, followed by multivariate analysis via binary logistic regression. **Results**: The mean age of the participants with stroke was 59.7 (SD:12.3) years. The prevalence of psychological distress among stroke patients was found to be 23.3% (95% CI:16.1–31.9). During bivariate analysis, six factors (p<0.05) were significant. The regression analysis identified five independent predictors: younger age (OR = 0.87, 95% CI = 0.79 - 0.97, p<0.05), female gender (OR = 70.94, 95% CI = 3.73 - 1348.89, p=0.05), patient being the sole source of income (OR = 24.71, 95% CI = 1.67 - 362.01, p<0.05), increased level of disability (OR = 13.05, 95% CI = 3.59 - 47.36, p<0.001), and past personal history of psychiatric disorders (OR = 172.59, 95% CI = 3.64 - 8174.42, p<0.05) with a  $R^2$  of 0.772. **Conclusion**: The prevalence of psychological distress among patients with stroke attending the Neurology Clinics of the NHSL, Colombo, is considerably high and is associated with multiple health and non-health related factors.

## Introduction

Stroke is one major cause of quality-of-life reduction. According to the American Heart Association, stroke is described as brain, spinal cord or retinal cell death from ischemia or hemorrhage based on symptoms persisting for >24 hours/death or pathological, radiological or objective evidence that is not attributable to trauma. Stroke is the second most common cause of death and the third most common cause of disability-adjusted life years lost worldwide. Regarding Sri Lanka, stroke is the sixth leading cause of death and the fifth leading cause of disability-adjusted life years lost.

Stress can be defined as an actual or perceived perturbation to an organism's psychological, resulting in the activation of coping mechanisms such as behavioral changes, activation of the sympathetic nervous system and adrenal medulla and secretion of stress hormones. Thus, distress denotes a negative state in which the coping mechanisms and adaptation processes have failed to return the organism to its normal state.<sup>4</sup>

Approximately one-third of post-stroke patients suffer from psychological distress (PsyD) worldwide.<sup>5</sup> A multitude of factors affect the prognosis of PsyD among post-stroke patients and, in the end, lead to poor outcomes such as limitation of daily activities, poor rehabilitation outcomes, social isolation, poor functional recovery, vascular events, and recurrent episodes of stroke.<sup>6</sup>

Most research found in the literature was found to be focused on the effect of either depression or anxiety on stroke patients rather than assessing the combined effect. Added to that was the use of specific rating scales to assess either the level of PSD (Poststroke depression) or PSA (Post-stroke anxiety), which was rather more sensitive in measuring the overall level of distress rather than an isolated condition. The conclusions of Schramke *et al.* (1998) state that "these results suggest the need for caution in using rating scales of depression and anxiety in neurologic patients and support the notion that these scales are sensitive to distress rather than specific for identifying depressive and anxiety disorders" supporting the validatory importance of a general approach to PsyD to avoid misinterpretations and inequity

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towards different groups within the same study population.<sup>8</sup> Furthermore, stroke-induced PsyD carries a greater risk of mortality, social impairment, and poor drug compliance, imposing detrimental effects on the quality of life of the patient and posing a long-lasting effect on the rest of the family as well.<sup>7</sup>

Hence, we believe that the psychiatric consequences of stroke are significant, especially in low-income settings comparable to those in developed countries, and we aim to have a holistic approach in this regard through the assessment of PsyD. The conduction of these studies can be used to identify the potential factors that can have possible implications beneficial in the local setting, as it allows future researchers to correlate local and international research evidence to improve the practical applications of findings. The conclusions thus derived can be used in Sri Lanka as well as in other lower middle-income countries to channel their limited resources for early detection and prevention, which is of higher feasibility than the medical management that follows progressed severe clinical depression. Furthermore, it is applicable in the busy clinic and ward schedules commonly seen, as clinicians will only be required to direct their specific psychiatric concerns towards a selected group of people with a potential tendency.

## **Methods**

# **Study Design**

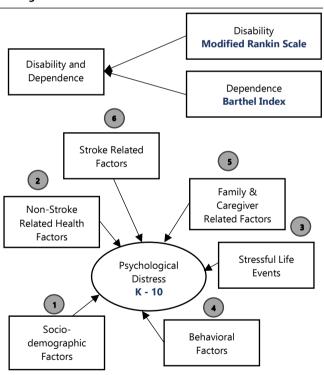
A descriptive cross-sectional study with an analytical component was conducted in the Neurology Clinics of the National Hospital of Sri Lanka (NHSL), Colombo, the largest tertiary care hospital in the country. The analytical component was incorporated to assess the prevalence of psychological distress amongst adult poststroke patients and, thereon, evaluate the factors influencing it in order to apply them, particularly in resource-poor clinical settings, pragmatically. The study period extended from April 2021 to December 2021 and data collection was carried out in September 2021. The study population was based on the adult post-stroke patients attending the Neurology Clinics of the study setting since long-term management of stroke is mainly based on an outpatient basis in the local context. Patients diagnosed with stroke who were above 18 years of age and had been diagnosed at least one month prior were included in the study. We excluded patients with significant language and cognitive impairment that will hinder the fidelity of the data, other severe disabilities unrelated to the stroke, such as loss of a limb and those severe mental illnesses (preceding the stroke) and confusion that impairs the capacity to give consent.

# **Sampling and Data Collection**

A probability-based systematic sampling method was initially decided to be used in this research. The first five stroke patients attending each clinic fulfilling the inclusion and exclusion criteria were given sequential numbers and one number to be selected via a random number generator as the first participant to be recruited from that clinic.

After that, every other patient satisfying the inclusion and exclusion criteria was to be recruited into the study until the required sample size was completed. However, due to the COVID-19 pandemic situation in the country during the period of data collection and practical difficulties imposed by the pandemic lockdown, the sampling method was switched to multistage random sampling. Accordingly, two of the four consultants holding Neurology Clinics, NHSL, Colombo, were randomly selected. After that, the clinic records of all the post-stroke patients attending their clinics were accessed. A list of patients with contact numbers conferring to the inclusion and exclusion criteria was formed under sequential numbers. After that, 180 patients were randomly selected using a random number generator (allocating 144 participants for entry and 36 patients considering a non-response rate of 20%). These patients were contacted via phone at a convenient time for the patient, and study instruments were administered upon the acquisition of informed consent.

Figure 1. Conceptual Framework for Psychological Distress Among Stroke Patients.



**Legend:** The presence of psychological distress assessed via K–10 was hypothesized to be influenced by factors under 6 domains (stroke and non-stroke-related health factors considered collectively as health factors). Blocks refer to the clusters of variables; solid arrows refer to expected causal effects; dashed arrows refer to components of a cluster; and text in bold refers to study instruments used. Data regarding the content numbered 1 – 6 were obtained from Section A of the questionnaire.

Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Colombo (MFC/AL/2017/1290), administrative clearance was acquired from

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the director of the National Hospital of Sri Lanka, Colombo, and permission was obtained from the consultants of all four neurology clinics.

## **Study Instruments**

The study instrument used comprised three sections, all of which were interviewer-administered to the participants. <u>Figure 1</u> None of the three sections involved any manuals requiring investigator training. However, the investigators discussed consistency, and advice was obtained from a consultant psychiatrist to gain insight regarding this process.

- Section A A questionnaire developed by the investigators under the supervision of a consultant psychiatrist to identify the various factors listed under the socio-demographic, health-related, stroke-related, behavioral, stressful life event, and family and caregiver factorial domains.
- Section B Interviewer-administered Kessler's psychological distress scale (K- 10), standardized and validated for the Sri Lankan population.<sup>9</sup>
- Section C Interviewer-administered 10-item Barthel Index, standardized and validated for the Sri Lankan population by Lekamwasam et al. (2011) and the modified Rankin scale.<sup>10</sup>

# **Data Analysis**

## **Dichotomization of the Dependent Variable**

Data was analyzed descriptively and analytically by the SPSS statistical software version 26. The validation of the K-10 to the Sinhala-speaking population of Sri Lanka by Wijerathne et al. (2005), presented a cutoff of ≥22 to categorize patients as 'distressed' or 'non-distressed', which was used to differentiate the distressed patients from the non-distressed patients.<sup>9</sup>

## **Descriptive Analysis**

The descriptive analysis of results was done using frequency distributions for basic sociodemographic and stroke-related details. Numerical variables were described via means and SDs, and categorical variables via proportions.

#### **Statistical Analysis**

Factors affecting PsyD were evaluated under several domains <u>Table 1</u>. Four domains that were not directly related to the patient's health were first analyzed, followed by two health-related domains (stroke-related and other health-related factors). Accordingly, two main statistical methods were used: bivariate analysis using chi-square tests and simple logistic regression, followed by multivariate analysis by multiple logistic regression. For each domain, categorical variables were subjected to initial bivariate analysis using Chi-square tests (and Fisher's exact tests when necessary) to identify the association between the factors of each domain on the level of PsyD. P-values of < 0.05 were considered statistically significant in all associations.

#### **Bivariate Analysis**

The bivariate analysis of continuous independent variables (age, number of stroke events, time since last stroke event, level of dependence on Activities of Daily Living, and level of disability) was carried out using simple logistic regression, where the results

*Table 1.* Classification of Variables Included in the Main Domains Assessed.

Socio-Demographic	Health Related	Stroke Related
Gender	Hypertension	Number of stroke events
Age	Dyslipidemia	Time since the last stroke event
Ethnicity	Diabetes Mellitus	Type of stroke
Highest Level of Education	History of Psychiatric Disorders prior to stroke	Dominance of the side affected
Monthly Household Income	Family History of Psychiatric Disorders	Follow-up care received
Employment Status	,	Membership of the stroke support group
Behavioral	Family and Caregiver	Stroke related Disability
Status of smoking	Marital status	Barthel Index
Frequency of smoking	Sole source of income	Modified Rankin Scale
Effect of stroke on frequency of smoking	Number of children	
Status of alcohol consumption	Presence of caregiver	
Frequency of alcohol consumption	Association with the caregiver	
Effect of stroke on	Time spent with the	
alcohol consumption	caregiver	
Status of engagement in physical/leisure activities		
Frequency of engagement in		
physical/leisure activities		
Effect of engagement in		
physical/leisure activities		
Status of religious activities		
Frequency of religious activities		
Effect of stroke on		
religious activities		

were presented in the form of odds ratio (OR) with 95% confidence intervals (95%CI) while considering  $\rho$  values <0.05 as significant. The level of PsyD persisted in becoming the dependent variable in all analyses.

# **Multivariate Analysis**

Under multivariate analysis, a hierarchical binary logistic regression analysis was carried out. Initially, age, gender, and history of psychiatric disorders were entered into the model since they were repeatedly identified in the literature as strong

confounders.<sup>11</sup> After that, the other independent predictors identified as significant using bivariate analysis were included in the second block, with the rest of the predictors in the third block to assess for confounding amongst variables in bivariate analysis. Predictors in the second and third blocks were added stepwise into the analysis process. Accordingly, after assessing multicollinearity and excluding any outliers, a final single model was formed by isolating the factors that are proven to be significant even after undergoing multivariate analysis (p < 0.05). The goodness-of-fit of the model was assessed using the Hosmer-Lemeshow test.

# **Results**

# **Study Sample**

The study included 177 subjects, with a response rate of 67.8 %. The participants' ages ranged from 27 to 91, with a mean age of 59.7 years, a standard deviation of 12.3 years, and a normal distribution. 27.5 % (n = 33) of the patients were employed, and 93.3% (n = 112) of the total sample had received formal secondary education. The majority of the participants had an ischemic stroke (85%, n = 102). The K-10 scores of the study sample ranged from 10 to 47 (the total range of the scale is 10-50), with a mean score of 16.7 and a standard deviation of 8.4, indicating an acceptably wide distribution. Based on the cut-off, 23.3% (n = 28) of the study sample was distressed.

# **Results of Bivariate Analysis**

Socio-demographic factors, the presence of at least one stressful life event, and family and caregiver-related factors did not possess statistically significant associations with PsyD according to the results of the bivariate analysis using chi-square tests and simple logistic regression (all p values > 0.05). The chi-square analysis revealed that history of psychiatric disease (p-value = 0.003), first-degree relatives with psychiatric diseases (p-value = 0.034) (under health-related factors), the frequency of engaging in physical/leisure activities prior to stroke (p-value < 0.05) (under lifestyle-related factors) to be significantly associated with PsyD. Under stroke-related factors, namely time since the last stroke event (p-value = 0.036, level of disability (p-value < 0.000), and level of dependence (p-value = 0.021) were significantly associated with PsyD during simple logistic regression (Table 2).

*Table 2.* Three Continuous Variables (Time Since the Last Stroke Event, Level of Dependence and Level of Disability) Associated with Psychological Distress Of Stroke Patients (N = 120).

Predictor	p	OR	95% CI
Time since last stroke event <sup>a</sup>	0.036	0.74	0.56 – 0.98
Level of Dependence <sup>b</sup>	0.021	0.99	0.97 – 1.00
Level of Disability <sup>c</sup>	p < 0.000	2.01	1.46 – 2.78

**Legend:** OR = Odds Ratio; CI = Confidence Interval; <sup>a</sup> Omnibus  $\chi^2$  (1) = 10.95,  $\rho$  < 0.05,  $R^2$  = 0.124 (Negelkerke); <sup>b</sup> Omnibus  $\chi^2$  (1) = 5.189,  $\rho$  < 0.05,  $R^2$  = 0.065 (Negelkerke), level of dependence regarding activities of daily living was assessed using the Barthel Index Score; <sup>c</sup> Omnibus  $\chi^2$  (1) = 21.195,  $\rho$  < 0.05,  $R^2$  = 0.248 (Negelkerke), level of disability was assessed based on the Modified Rankin Scale.

#### **Results of Multivariate Analysis**

The multivariate logistic regression analysis showed a statistically significant influence of younger age (p-value = 0.010), female gender (p-value = 0.005), presence of a history of psychiatric disease (p-value = 0.009), being the sole source of income to the family (p-value = 0.019) and increasing level of disability (p-value < 0.001) on the presence of PsyD ( $\chi 2$  (5) = 68.0,  $\rho$  < 0.001). The model was checked and cleared of potentially significant outliers. The variance inflation factors of the five predictors during the collinearity statistics were 1.045, 1.166, 1.064, 1.159 and 1.094, respectively, well below the standard cutoff for significant correlation between predictors. (1: no correlation, 1 – 5 moderate correlation with no significant impact on the model, >5: severe correlation with imprecise model) The Hosmer-Lemeshow Goodness-of-fit test for the model displayed a  $\chi^2$  (8) = 4.1 and p = 0.852, and the Omnibus Chi-square value was  $\chi^2$  (5)= 68.0 with a p-value < 0.001. The overall prediction percentage of the model was 92.6%, well above the standard cutoff of 80%. The model explained 77.2% of the variance (Negelkerke  $R^2$ ) with a sensitivity of 73.3% and specificity of 96.6% (Table 3).

Table 3. Results of the Multivariate Regression Analysis (n = 112) on Predictors of Psychological Distress.

Predictor	p	Unadjusted OR	Adjusted OR	95% CI
History of Psychiatric Disorders <sup>a</sup> , Yes	0.009	5.15	172.59	3.64-8174.42
Age	0.01	-0.13	0.87	0.79-0.97
mRS	<0.001	2.57	13.05	3.59-47.36
Gender <sup>b</sup> , Female	0.005	4.26	70.94	3.73-1348.89
Sole Source of Income <sup>c</sup> , Yes	0.019	3.21	24.70	1.67-362.01
Constant	0.045	-4.77	0.008	

**Legend:** OR = Odds Ratio; CI = Confidence Interval; mRS = modified Rankin Scale; Omnibus  $\chi^2$  (5) = 68.022,  $\rho$  < 0.001,  $R^2$  = 0.772 (Negelkerke). Reference levels of the independent categorical levels. <sup>a</sup> absence of a history of psychiatric diseases; <sup>b</sup> male gender; <sup>c</sup> Not the sole source of income

## Discussion

This study was carried out to assess the prevalence and the associated factors of PsyD among the post-stroke patients attending the Neurology Clinics of the NHSL, Colombo. The cross-sectional study design facilitated the investigators to compare distressed and non-distressed patients and the strength of each factor in its influence on the presence of psychological. The prevalence of PsyD in the current study is comparable to that reported in other local and international studies. The differences could be attributed to the differences in the sample sizes, age

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ranges of participants and other restrictions in inclusion criteria.  $^{8,12,13}$ 

Under the different variables, factors like age and gender were frequently discussed in past studies with contrastingly different results, with some presenting young age as a risk factor and others as a protective factor or as insignificant. However, in the present study, age was recognized as statistically significant in the final binary logistic regression model (OR = 0.87: 95% CI: 0.79 - 0.97; p = 0.010). This might confirm the findings of the systematic review by Hackett and Anderson (2005), where age is considered a crucial demographic factor that is to be mandatorily included in multivariate analysis. <sup>11</sup> Thus, the contrasting findings in different studies might be due to the confinement to bivariate analysis in most studies and not including multivariate analyses.

In the current study, gender was not found to have a statistically significant influence on PsyD in the initial bivariate analysis. In contrast, female gender was found to be significant in multivariate analysis. Similarly, 13 out of 21 studies reviewed by Robinson and Jorge, 2016, did not find gender as a significant predictor of PSD in their initial analyses.<sup>14</sup>

Studies by Ferro et al., 2016 and Mirolovics et al., 2020, indicate higher educational levels as a protective factor for PsyD, which was not identified by this study either in bivariate or multivariate analysis. <sup>15,16</sup> This could be attributed to differences in the study samples, precisely due to lower proportions of participants with lower educational levels, which could have affected the findings (the proportion of participants with an educational level less than Grade 5 was 6.7%).

The current study did not identify income level as a significant predictor of PsyD, which differed from studies conducted by Mirolovics et al., 2020, which recognized higher economic status as associated with lower PsyD.<sup>15</sup> This association could have been due to the costs of medication and the acquisition of health facilities, which play a significant role in the long-term management of stroke. However, this might not be relevant in the local setting due to the presence of a free health care service in the country, which indicates the non-significant results.

Furthermore, a study conducted in China identified hypertension to be significantly associated with PsyD in both bivariate and multivariate analyses. However, none of these factors were found to have a statistically significant association with PsyD in the present study. In the Chinese study, only young patients in the age range of 20 to 44 years were considered, which could have had a significant influence on the results, as the presence of other chronic conditions will significantly impact younger patients, being an economically driving force in all societies in addition to the stroke itself. This is further gratified by the absence of age adjustment in none of the regression models where hypertension was statistically significant (model for the Symptom Checklist 90 Revised and the model for anxiety).

A meta-analysis carried out by Mitchell et al., 2017, identified both past personal and family history of depression as crucial risk factors for post-stroke depression, adjustment disorder and anxiety.<sup>17</sup> Even though a family history of psychiatric disorders was statistically significantly associated with PsyD only in the initial bivariate analysis in this study, significant results were found regarding past personal history of psychiatric disorders in both bivariate and multivariate analyses.

When considering behavioural factors, a Norwegian study exploring the association between pre-stroke physical activity with symptoms of anxiety and depression three months poststroke identified higher activity levels prior to the stroke event to be protective against post-stroke depression in their multivariate analysis despite 41.5% of the study population, not having a significant reduction or increase in the level of physical activity following the stroke event. This contrasts with the present study, which found no significant association between engagement in physical activities prior to the stroke event and the presence of PsyD. However, the frequency of physical activities prior to the stroke event was significantly associated with PsyD in the bivariate model (it was not included in the final regression model due to the effects of multicollinearity). Here, higher frequencies of physical activity prior to the stroke event were associated with the presence of distress, which could be associated with mental stress in such patients due to the limitation of activity following the disabilities imposed on them by the cerebrovascular accident. However, other factors under this domain specifically included to suit the local cultural setting but not openly discussed in the literature, such as religious activities, were insignificant in their results.

Under family and caregiver factors, although specific studies state the importance of family members and friends in relieving the internal isolation experienced by patients, a quantitative analysis of this using the marital status, number of family members and dependents was insignificant.<sup>18</sup>

Stroke-related factors were considered to be among the most highly debated in the literature. For example, regarding the time since the last stroke event, some studies presented that depressive symptoms decreased with the time since the stroke, while others expressed otherwise. In the initial bivariate analysis of this study via simple logistic regression, an increase in the time since the last stroke event (in years) was associated with a reduction in PsyD (OR = 0.74; 95% CI:0.56 - 1).

Unlike other factors of the same domain, stroke-related disability and dependence on Activities of Daily Living (ADL) were both consistently associated with higher levels of distress and depression in post-stroke patients. The systematic review by Hackett and Anderson (2005) identifies disability status to be a factor that both researchers and clinicians should prioritize in the detection of depression among post-stroke patients. <sup>11</sup> Similarly, disability status assessed by the modified Rankin scale was identified to be a statistically significant predictor of PsyD in both bivariate and multivariate analysis in the current study (p < 0.001).

Accordingly, these factors identified can be utilized at the point of discharge in the early rapid recognition of patients for referrals and during follow-up care so that limited psychiatric resources could be efficiently channeled to prioritize patients at a comparatively high level of risk.

Throughout the interpretation of the results of the final logistic regression model, the wide confidence intervals obtained for the different predictors, particularly for the presence of a history of psychiatric disorders, female gender, and the being the sole source of income, even after assessments for multicollinearity and outliers should be given due significance. While it is in congruence with the similar findings in the literature discussed above with powerful associations established with the dependent variable, imprecision due to small size should always be considered and noted.

Notably, there were several limitations in the study with relevance to (1) the inability to obtain an adequate sample size due to pragmatic issues from the pandemic situation which could potentially have had a significant impact on the statistical analysis as well, (2) low response rate of 67.79%, (3) absence of temporal associations between the predictors and outcomes due to the study design, (4) inability to generalize findings outside the study setting due to the absence of multiple center involvement in the study setting, (5) inability to assess the added impact of the CoVID-19 pandemic on patients, (6) change in the sampling method to multistage random sampling and data collection via phone calls over direct face-to-face interviews due to the pandemic. Hence, further research should be encouraged, particularly by incorporating clinical assessment into the screening tools in assessing PsyD and by including details regarding stroke subtype classifications and stroke severity assessments via radiological and clinical data. Furthermore, such studies should be expanded to a multicenter level and incorporate direct investigator-participant interactions to reduce bias and expand generalizability. Moreover, it will be essential to explore the challenges faced by post-stroke patients who are not psychologically distressed and the factors that influence poor outcomes in them as well.

#### Conclusion.

In conclusion, this study conducted to make a holistic approach to the psychological consequences of stroke on patients revealed a significant prevalence of PsyD amongst post-stroke patients in the outpatient setting and was associated with several health and non-health related factors. These findings, comparable with international studies, shed light on the Sri Lankan perspective and have a multitude of clinical implications in the long-term care of these patients, especially in low-income settings. However, several limitations, owing to the pandemic situation in which the study was conducted and the inherent characteristics of the design itself, direct potential for further research on this topic. Nevertheless, this study landmarked as potentially the first of its kind in Sri Lanka, for the best of our knowledge can direct the course of neuropsychiatric care of post-stroke patients by clinical transcending beyond and sociodemographic characteristics to include caregiver as well as family-related data to identify patients at risk.

# **Summary – Accelerating Translation**

Prevalence and Associated Factors of Psychological Distress of Patients with Stroke Attending a Neurology Clinic – A Descriptive Cross-sectional Study

Aims: To assess the prevalence of psychological distress and identify its associated factors among the post-stroke patients attending the Neurology Clinics of the National Hospital of Sri Lanka (NHSL), Colombo. Background – A multitude of factors affect the prognosis of psychological distress among post-stroke patients. Existing studies have primarily focused on post-stroke anxiety or depression using non-specific scales. These scales may not fully represent the outcomes. Even though many factors are known to be associated with psychological distress, there are many controversies regarding many factors. Very few studies have accounted for the effects of confounding in their analysis in identifying potential predictors.

Outcomes of the Study – Psychological distress is a significant issue in the current context, accounting for approximately ¼ of the post-stroke patients. Age, gender, being the sole source of income, history of psychiatric disorders and the level of disability assessed by the modified Rankin Scale were identified as statistically significant predictors of psychological distress via binary logistic regression analysis.

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#### **Author Contributions**

Methodology, Investigation, Visualization: PW, CW, NW & IM; Data Curation: PW, CW & NW; Resources: PW, NW & IM; Writing – Original Draft: PW & NW; Formal Analysis, Software: PW; Supervision: IM; Project Administration: PW & IM. Writing – Review & Editing: PW, CW, NW & IM.

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