ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Risk factors of post-stroke depression after acute ischemic stroke - A prospective study from a tertiary care hospital in South India

Roy Thomas

Associate Professor, Department of Neurology, Travancore Medical College Hospital, Kollam, Kerala, India

Submission: 05-06-2023 Revision: 31-09-2023 Publication: 01-11-2023

ABSTRACT

Background: Post-stroke depression is a major cause for poor functional and rehabilitation recovery. **Aims and Objectives:** The aims of the study were to determine risk factors causing depression in acute ischemic stroke. **Materials and Methods:** Prospective cohort study was conducted in acute ischemic stroke patients between January 2023 and April 2023 at Travancore Medical College, Kerala. They were divided into – ischemic stroke patients with depression and without depression. Variables studied – age, gender, marital, educational, occupation, socioeconomic status, national institute of health stroke scale (NIHSS) at admission, modified Rankin Scale (mRS) at 1 month, stroke lateralization, risk factors, and lobe and site. **Results:** Among 270 patients, 164 (60.7%) were male, 254 (94.1%) were above 50 years, 250 (92.6%) had marriage partner, 164 (60.7%) unemployed, 138 (51.1%) belonged to middle socioeconomic status, and 172 (63.7%) from rural areas. About 91 (33.7%) were in ischemic stroke patients with depression group. In univariate analysis, marriage, socioeconomic status, subcortical location, left hemisphere, severe NIHSS, and high mRS were associated with post-stroke depression. In multivariate analysis, socioeconomic status, subcortical location, and left hemisphere were significant risk factors. Strongest predictor was subcortical location. **Conclusion:** Early identification of following risk factors – socioeconomic and marital status, subcortical location, left hemisphere lesion, severe NIHSS, and high mRS in acute stroke patients may help to identify those who are vulnerable for post-stroke depression.

Key words: Cerebrovascular disorder; Mood disorder; Risk factor; Vascular depression

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i11.55354

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Depression is observed in at least one-third of stroke patients.[1] This will indeed result in poor functional outcome and higher mortality.[2,3] There is great variability in post-stroke depression – the prevalence ranging from 17% to 73%.[4] These rates, however, show no variation on time period of presentation – be it less than a month, 1–6 or 6–12 months. It also does not vary on the setting (population, hospital, or rehabilitation). The highest frequency is reported at any time within the 1st year, and thereafter, it shows a declining trend.[1]

The pathophysiology of depression in stroke patients is complex. The causes attributed are multifactorial. It has biological and psychosocial components. This varies according to the timing of the presentation. It may be due to the psychological reaction to cognitive and functional neurological deficits. The psychosocial factors causing post-stroke depression and depression alone are similar. They include past psychiatric problems, neurotic traits, and social aloofness.[5]

Evidence suggests that post-stroke depression has underlying biological components. This was not only a psychological consequence to a new deficit. It was noted that depression was more common post-stroke when compared to illness with similar levels of disability.[6] The biological factors attributed were location of infarct, genetic susceptibility, inflammation, neuroplasticity, neurotrophic

Address for Correspondence:
Dr. Roy Thomas, Associate Professor, Department of Neurology, Travancore Medical College Hospital, Kollam, Kerala, India.
Mobile: +91-9495309187. **E-mail:** drroythom@yahoo.com

components, dysfunction of cortico-striato-pallido-thalamic-cortical pathways, and variations in dopaminergic, serotonergic, and noradrenergic neurotransmitters which result in alteration in amine levels.[7]

Observational studies have detected predictors of post-stroke depression. History of mental illness, gender, age, neuroticism, family history, severity of stroke, and level of handicap had a positive association with occurrence of post-stroke depression.[8] Other psychological risk factors identified are anxiety and lack of family and social support.[9] Old age, females, diabetes mellitus, subtype of stroke, living alone, education level, and past history of stroke have shown varying results in other studies.[2]

The various studies show inconsistent findings and there have been no recent prospective studies published from Kerala. Hence, a prospective study on post-stroke depression was conducted. The aim of this study was to determine the clinical features and risk factors causing depression in early acute ischemic stroke patients. The following risk factors were considered to be analyzed in this study – age, gender, marital, educational, occupation, socioeconomic status, national institute of health stroke scale (NIHSS) at admission, modified Rankin scale (mRS) at 1 month, stroke lateralization, risk factors, and lobe and site involved of ischemic stroke. Early identification of these risk factors would help to identify vulnerable patients and help in better care and rehabilitation.

Aims and objectives

To determine the clinical features and risk factors causing depression in early acute ischaemic stroke patients.

MATERIALS AND METHODS

This was a prospective observational study conducted over a period of 4 months between January 2023 and April 2023. The study was conducted at a Travancore Medical College Hospital, Tertiary Care Center in Kerala. This study was approved by the Institutional Research and Ethics Committee review board (TMC-IEC:-132/23). A total of 270 adult patients who presented with acute ischemic stroke during the study period were included in this study. Written informed consent was taken for participation in this study. Patients were recruited by consecutive non-random sampling. A semi-structured pro forma was used to collect the data. Acute stroke is brain cell death attributable to ischemia based on pathological, imaging, or other objective evidence of cerebral ischemic injury in a defined vascular distribution.

All adult patients who were diagnosed to have acute ischemic stroke were included in the study. The following patients with primary hemorrhagic stroke, previous stroke, significant cognitive or comprehension disorder, on anti-depressant medications, premorbid depression, severe speech impairment, dementia, and other psychiatric disorder were excluded from the study.

Patients with acute ischemic stroke were diagnosed using ICD 11 criteria for depression and rated using the 17-item Hamilton depression rating scale (HAMD) questionnaire at 1 month after the onset of ischemic stroke.[10,11] HAMD for scoring was used to assess the severity of depression. This is a 17-item scale with maximum score of 52. Score 0–7 is normal, 8–16 mild depression, 17–23 moderate depression, and >24 is considered to have severe depression.[11]

The patients were divided into two groups – ischemic stroke patients with depression and ischemic stroke patients without depression. The variables studied would be the following – age, gender, marital status, educational status, occupation, socioeconomic status (Modified Kuppuswamy Socioeconomic Scale),[12] NIHSS at admission,[13] mRS at 1 month,[14] stroke lateralization, lobe and site involvement, and risk factors for stroke.

Statistical analysis

All statistical analysis was done using the Statistical Package for the Social Sciences statistics (IBM corporation, Armonk, New York), version 27.0. Quantitative variables were expressed as mean±standard deviation, whereas qualitative variables were expressed as frequencies and percentages. Comparison between groups (with and without depression) was performed using the Chi-square test. Significant factors that were designated as being associated with depression using the univariate analysis were entered in the multivariable logistic regression analysis to identify the risk factors. Measures of association were expressed as odds ratio (OR) and 95% confidence interval (CI). P≤0.05 was considered significant.

RESULTS

Among 270 patients diagnosed with acute ischemic stroke, 91 (33.7%) were in stroke patients with depression group and 179 (66.3%) were in stroke patients without depression group.

Demographics

In the study, 164 (60.7%) were male and 106 (39.3%) were female. Two hundren and fifty-four patients (94.1%) were above 50 years of age. Regarding marital status, 250 (92.6%) had a marriage partner while 20 (7.4%) were of single status (unmarried, widow, and divorced). The

majority of the patients in this study were literate (90.4%), unemployed (60.7%), belonged to middle socioeconomic status (51.1%), and lived in rural areas (63.7%). Among the other demographic factors studied, socioeconomic status and marital status were statistically significant when compared between the two groups (Table 1).

Stroke risk factors

The distribution of risk factors for stroke – diabetes, hypertension, dyslipidemia, coronary artery disease, atrial fibrillation, smoking, alcohol, and family history of depression was nearly the same between the two groups (Table 2).

Location, site, territory, and lobe and severity

Post-stroke depression was seen in 67.9% of patients with subcortical lesions which were significantly high when compared to 12.7% of patients in cortical group. About 66.3% of the patients with left-sided lesion had post-stroke depression, whereas only 20% had post-stroke depression among the right-sided lesion group. In context to the severity of stroke, severe NIHSS (score >10) and high mRS (3–5) were more common in the post-stroke depression group (Table 3).

Severity of depression

Among 91 patients with post-stroke depression, 21 (23%) were found to have severe depression, 57 (63%) had moderate, and 13 (14%) had mild depression based on HAMD scale (Figure 1).

In univariate analysis, marriage, socioeconomic status, subcortical location, left hemisphere, severe NIHSS score, and high mRS score were associated with the development of post-stroke depression. Multivariate analysis was done to assess the independent factors. In multivariate analysis, socioeconomic status, subcortical location, and left hemisphere lesion were significant risk factors for post-stroke depression. The strongest predictor for post-stroke depression was subcortical location (OR=2.66) (Tables 4 and 5).

Table 1: Demographics in stroke patients with depression and without depression

	Depression (n=91) (%)	No depression (n=179) (%)	P-value
Age			
<50 years	2 (2.2)	14 (7.8)	0.0643
>50 years	89 (97.8)	165 (92.8)	
Gender			
Male	54 (59.3)	110 (61.5)	0.7369
Female	37 (40.7)	69 (38.5)	
Marriage			
Married	80 (87.8)	170 (94.9)	0.0179*
Single status-unmarried	1 (1.1)	4 (2.2)	
Single status-widow/divorced	10 (11.1)	5 (2.9)	
Socioeconomic status			
Lower	50 (54.9)	68 (37.9)	0.0226*
Middle	36 (39.6)	102 (56.9)	
Upper	5 (5.5)	9 (5.2)	
Education			
Illiterate	9 (9.9)	17 (9.5)	0.9176
Literate	82 (90.1)	162 (90.5)	
Job status			
Employed/Pensioner	33 (36.2)	73 (40.8)	0.4723
Unemployed	58 (63.8)	106 (59.2)	
Residence			
Urban	32 (35.2)	66 (36.9)	0.7827
Rural	59 (64.8)	113 (63.1)	

*P<0.05-Statistically significant

Table 2: Stroke risk factors in patients with depression and without depression

Risk Factors	Depression (n=91) (%)	No depression (n=179) (%)	P-value
Diabetes	62 (68.1)	123 (68.7)	0.9223
Hypertension	73 (80.2)	143 (79.9)	0.9486
Dyslipidemia	41 (45.1)	77 (43.1)	0.7496
Coronary artery disease	9 (9.9)	22 (12.3)	0.5586
Atrial Fibrillation	8 (8.8)	20 (11.2)	0.5439
Smoking	50 (54.9)	106 (59.2)	0.5016
Alcohol	49 (53.8)	102 (56.9)	0.6235
Family history of depression	7 (7.7)	17 (9.5)	0.6222

Table 3: Comparison between location, site, territory, and lobe and severity between stroke patients with depression and without depression

Location	Depression (n=91) (%)	No depression (n=179) (%)	P-value
Supratentorial			
Cortical	6 (6.6)	43 (24.1)	0.0004**
Subcortical	70 (76.9)	103 (57.5)	0.0017**
Infratentorial			
Brain stem	8 (8.8)	16 (8.9)	0.9679
Cerebellum	7 (7.7)	17 (9.5)	0.2427
Site			
Left hemisphere	63 (69.2)	32 (17.9)	<0.0001**
Right hemisphere	21 (23.1)	84 (46.9)	
Both	7 (7.7)	63 (35.2)	
Territory			
ACA	5 (5.5)	12 (6.7)	0.7343
MCA	70 (76.9)	129 (72.1)	
PCA	16 (17.6)	38 (21.2)	
Lobe			
Frontal	24 (26.4)	53 (29.6)	0.3098
Non frontal	67 (73.6)	126 (70.4)	
NIHSS			
Mild (0–3)	3 (3.3)	63 (35.2)	<0.0001
Moderate (4–10)	43 (47.3)	75 (41.9)	0.4018
Severe (>10)	45 (49.4)	41 (22.9)	<0.0001**
mRS			
0–2	51 (56.1)	126 (70.4)	0.0190*
3–5	40 (43.9)	53 (29.6)	

*P<0.05-statistically significant, **P<0.001-statistically highly significant

Table 4: Comparison between involvement of subcortical structures and severity of depression

Depression	Mild (%)	Moderate (%)	Severe (%)	Total (%)	P-value
Basal ganglia	5 (7.1)	14 (20)	6 (8.6)	25 (35.7)	0.5540
Thalamus	2 (2.9)	7 (10)	3 (4.3)	12 (17.2)	0.8740
Internal capsule	4 (5.7)	24 (34.3)	5 (7.1)	33 (47.1)	0.3793
Total	11 (15.7)	45 (64.3)	14 (20)	70 (100)	

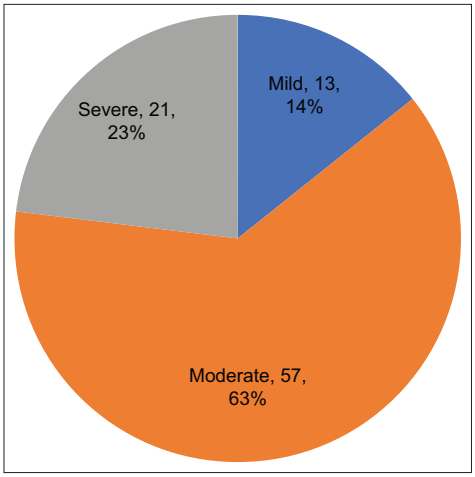

Figure 1: Based on the severity of depression

DISCUSSION

Post-stroke depression is a common sequelae to stroke that can interfere with the functional recovery and quality of life. Incident depression post-stroke is considered to be an independent risk factor for mortality from natural and unnatural causes.[15] Only few prospective studies have analyzed the risk factors contributing to post-stroke depression. Although few have proposed a predictive model, none were replicated to an independent population of stroke patients.[16]

In this study, post-stroke depression within 1 month of early stroke onset was observed in 33.7% of stroke patients. In the Chinese study by Zhang et al., the prevalence of post-stroke depression was 27.47% in the early post-stroke period.[17] In Danish study by Jørgensen et al., 25.4% had depression within 2 years after stroke with more than half of cases within a month.[15] In a study by Mohammed et al., in Egypt, the prevalence was as high as 60.78% within 3 months of stroke onset.[18] In meta-analysis by Ayerbe et al., patients who developed depression in 5 years post-stroke ranged from 39% to 52%.[16] Differences in reported prevalences of various studies are likely a result of differences in methods of measurement and a function of timing of evaluation.

Table 5: Independent risk factors associated with post-stoke depression identified by multivariable regression analysis

Variables	OR	95% CI		P-value
		Lower	Upper	
Marriage				
Single status	1.45	0.45	4.61	0.5260
Socioeconomic status				
Lower	1			0.0032**
Middle	0.36	0.18	0.71	
Upper	0.65	0.16	2.59	
Location				
Cortical	2.46	0.71	8.56	0.1547
Subcortical	2.66	1.06	6.68	0.0370*
Site				
Left hemisphere	1			<0.0001**
Right hemisphere	0.15	0.07	0.31	
Both	0.04	0.01	0.12	
Stroke severity				
NIHSS >10	1.93	0.99	3.42	0.0610
mRS 3–5	1.84	0.94	3.59	0.0713

*P<0.05-statistically significant, **P<0.001-statistically highly significant, CI: Confidence interval

In this study, gender and age did not reveal any significant association with post-stroke depression. This was in accordance with the studies by Mohammed et al.,[18] In the study by Zhang et al., there was a higher incidence in females with no significance with age.[17] In the study by Jørgensen et al., older age and female sex were observed with higher rate of depression.[15]

In this study, marital status and socioeconomic status influenced the development of post-stroke depression. This was not seen in Zhang et al., study.[17] Single cohabitation status was associated with higher rate of depression in Jørgensen et al., study.[15] The sociocultural pattern variability among different countries may be the reason for the same. Literacy, employment, and rural-urban settlement did not have any influence in this study. In a recent study by Al Qawasmeh et al., when compared with illiterate patients, those with secondary and high school education levels were less likely to get depression.[19]

The major risk factors for stroke etiology studied were diabetes, hypertension, dyslipidemia, coronary artery disease, atrial fibrillation, smoking, alcohol, and family history of depression. However, there was no significant relationship between these risk factors and depression in post-stroke patients in this study. In the study by Mohammed et al., hypertension and smoking were significant risk factors for post-stroke depression.[18]

In this study, left hemispheric lesion and subcortical location were significant risk factors for post-stroke depression. This was in concurrence with the study by Sam et al., and Zhang et al.,[17,20] Lesion location has been extensively studied as a causative factor for post-stroke depression. The findings, however, have been inconsistent. It has been reported that acute stroke patients with left basal ganglia or left frontal lesions had a significantly higher frequency of depression than with other lesion locations. Subsequent analysis revealed that this association appears to be a transient and remains significant only during the first 6 months after stroke.[21]

In this study, patients with post-stroke depression had a significant functional disability (NIHSS and mRS) compared to stroke patients without depression. This was consistent with many previous studies that had reported a significant relationship between disability and post-stroke depression.[17,18] There was a stepwise increase in the risk of depression after stroke for increased stroke severity.[15]

An early identification of the following risk factors – socioeconomic and marital status, subcortical location, left hemisphere, severe NIHSS score, and high mRS score in acute stroke may help to identify those patients who are vulnerable for post-stroke depression. Starting early psychosocial therapies in such patients may prevent the development of post-stroke depression, thus enabling a better recovery in them.

Limitations of the study

The conclusions were based on observation from a single study center. Furthermore, the sample size was relatively low. Thus, a prospective multicentre study is required to further evaluate the risk factors.

CONCLUSION

Socioeconomic status, left hemisphere, and subcortical location are significant risk factors for resulting in post-stroke depression. In view of the unfavorable impacts of post-stroke depression, it is essential to identify these to negate their impacts in stroke patients.

ACKNOWLEDGMENT

Nil.

REFERENCES

1. Hackett ML and Pickles K. Part I: Frequency of depression after stroke: An updated systematic review and meta-analysis of observational studies. Int J Stroke. 2014;9(8):1017-1025. https://doi.org/10.1111/ijs.12357
2. Kutlubaev MA and Hackett ML. Part II: Predictors of depression after stroke and impact of depression on stroke outcome: An updated systematic review of observational studies. Int J Stroke.

2014;9(8):1026-1036.
https://doi.org/10.1111/ijs.12356

3. Bartoli F, Lillia N, Lax A, Crocamo C, Mantero V, Carrà G, et al. Depression after stroke and risk of mortality: A systematic review and meta-analysis. Stroke Res Treat. 2013;2013:862978.
https://doi.org/10.1155/2013/862978
4. Kaadan MI and Larson MJ. Management of post-stroke depression in the Middle East and North Africa: Too little is known. Neurol Sci. 2017;378:220-224.
https://doi.org/10.1016/j.jns.2017.05.026
5. Wang Z, Shi Y, Liu F, Jia N, Gao J, Pang X, et al. Diversiform etiologies for post-stroke depression. Front Psychiatry. 2019;9:761.
https://doi.org/10.3389/fpsyt.2018.00761
6. Towfighi A, Ovbiagele B, El Husseini N, Hackett ML, Jorge RE, Kissela BM, et al. Poststroke depression: A scientific statement for healthcare professionals from the American heart association/ American stroke association. Stroke. 2017;48(2):e30-e43.
https://doi.org/10.1161/STR.0000000000000113
7. Lai YJ and McCullough LD. Poststroke depression: Pathophysiology and treatment strategies. In: Neurobiology of Depression. Cambridge: Academic Press; 2019. p. 197-205.
https://doi.org/10.1016/B978-0-12-813333-0.00018-4
8. Shi Y, Yang D, Zeng Y and Wu W. Risk factors for post-stroke depression: A meta-analysis. Front Aging Neurosci. 2017;9:218.
https://doi.org/10.3389/fnagi.2017.00218
9. De Ryck A, Brouns R, Geurden M, Elseviers M, De Deyn PP and Engelborghs S. Risk factors for poststroke depression: Identification of inconsistencies based on a systematic review. J Geriatr Psychiatry Neurol. 2014;27(3):147-158.
https://doi.org/10.1177/0891988714527514
10. Sharp R. The Hamilton rating scale for depression. Occup Med (Lond). 2015;65(4):340.
https://doi.org/10.1093/occmed/kqv043
11. Stein DJ, Szatmari P, Gaebel W, Berk M, Vieta E, Maj M, et al. Mental, behavioral and neurodevelopmental disorders in the ICD-11: An international perspective on key changes and controversies. BMC Med. 2020;18(1):21.
https://doi.org/10.1186/s12916-020-1495-2
12. Sood P and Bindra S. Modified Kuppuswamy socioeconomic scale: 2022 update of India. Int J Community Med Public Health. 2022;9(10):3841-3844.
https://doi.org/10.18203/2394-6040.ijcmph20222581
13. Lyden P. Using the national institutes of health stroke scale: A cautionary tale. Stroke. 2017;48(2):513-519.
https://doi.org/10.1161/strokeaha.116.015434
14. Broderick JP, Adeoye O and Elm J. Evolution of the modified rankin scale and its use in future stroke trials. Stroke. 2017;48(7):2007-2012.
https://doi.org/10.1161/strokeaha.117.017866
15. Jørgensen TS, Wium-Andersen IK, Wium-Andersen MK, Jørgensen MB, Prescott E, Maartensson S, et al. Incidence of depression after stroke, and associated risk factors and mortality outcomes, in a large cohort of Danish patients. JAMA Psychiatry. 2016;73(10):1032-1040.
https://doi.org/10.1001/jamapsychiatry.2016.1932
16. Ayerbe L, Ayis S, Wolfe CD and Rudd AG. Natural history, predictors and outcomes of depression after stroke: Systematic review and meta-analysis. Br J Psychiatry. 2013;202:14-21.
https://doi.org/10.1192/bjp.bp.111.107664
17. Zhang WN, Pan YH, Wang XY and Zhao Y. A prospective study of the incidence and correlated factors of post-stroke depression in China. PLoS One. 2013;8(11):e78981.
https://doi.org/10.1371/journal.pone.0078981
18. Mohammed GF, Azab HM, Sayed MA, Elnady HM, Youssif H and Mahmoud OA. Risk factors for post-stroke depression in Sohag University Hospital. Egypt J Neurol Psychiatry Neurosurg. 2019;55:11.
https://doi.org/10.1186/s41983-019-0057-z
19. Al Qawasmeh M, Aldabbour B, Abuabada A, Abdelrahman K, Elamassie S, Khweileh M, et al. Prevalence, severity, and predictors of poststroke depression in a prospective cohort of Jordanian patients. Stroke Res Treat. 2022;2022:6506326.
https://doi.org/10.1155/2022/6506326
20. Sam SP, Geo J, Lekshmi GI and Kallivayalil RA. Post stroke depression and lesion location: A hospital based cross-sectional study. Kerala J Psychiatry. 2020;33(2):158-161.
https://doi.org/10.30834/KJP.33.2.2020.223
21. Robinson RG and Jorge RE. Post-stroke depression: A review. Am J Psychiatry. 2016;173(3):221-231.
https://doi.org/10.1176/appi.ajp.2015.15030363

Authors' Contributions:
RT- Definition of intellectual content, literature survey, prepared the first draft of manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation, and submission of article

Work attributed to:
Department of Neurology, Travancore Medical College Hospital, Kollam, Kerala, India.

Orcid ID:
Roy Thomas - https://orcid.org/0009-0009-3432-172X

Source of Support: Nil, **Conflicts of Interest:** None declared.