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A Study of the Association Between Post-Stroke Depression and Lesion Type, Laterality and Location

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Abstract

Stroke is one of the major causes of morbidity and mortality worldwide. Post-stroke neuropsychiatric manifestations are commonly seen and are associated with poorer functional outcome and quality of life. Depression is one of the most prevalent post-stroke neuropsychiatric manifestations, occurring in about 55% patients. Studies have shown that some neuroanatomical variables are more commonly associated with the occurrence of depression in the post-stroke period. This study attempted to find the association between cerebrovascular lesion variables and depression. Forty four subjects with the history of first ever stroke, with duration after stroke being >2 weeks and <1 year, were interviewed using a semi-structured proforma. Variables of stroke lesion type, laterality and location were collected using Magnetic Resonance Imaging (MRI). Depression was assessed using the DSM-5 TR criteria for Major Depressive Disorder and severity of depression was measured using the Hamilton Depression Rating Scale (HDRS). Level of independence in the activities of daily living (ADLs) was assessed using the Barthel Index(BI). Post-stroke depression was diagnosed in 27(61.4%) patients of stroke. Out of 44 patients of stroke, 76.9% patients with a left sided cerebrovascular lesion and 76% with a frontal lobe lesion were diagnosed with post-stroke depression (PSD). PSD was found to be significantly higher in patients with a left hemispheric lesion and involvement of the frontal cortex. However, lesion size did not show any significant difference in Post-stroke depression.

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Key Words

Neuropsychiatric, manifestations, prevalent, variables

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INTRODUCTION

Stroke is characterised by an acute focal injury in the nervous system occurring due to a vascular cause[1]. It is a leading cause of disability and mortality worldwide. Major Depressive Disorder is characterised by depressed mood, loss of interest, sleep and appetite disturbances, fatigue and loss of energy, causing socio-occupational dysfunction[2]. Post-stroke neuropsychiatric manifestations, including depression, anxiety, apathy and cognitive impairment increase the risk of functional disability and mortality[3]. Depression is a common phenomenon occurring after stroke with prevalence rates ranging from 18%-61%[4]. Hypotheses explaining the pathophysiology of depression after cerebrovascular injury include the disturbance in physiological system of biogenic amines, increased blood and CSF concentration of inflammatory cytokines and serotonin gene polymorphism[5].

Other factors that have been identified as risk factors for the development of post stroke depression include older age, female gender, previous history of depression, higher level of physical disability, cognitive impairment and poor social support[6]. A recent metaanalysis reported that the prevalence of depression at any time after stroke is about 29%[7]. According to an extensive cohort study, the number of individuals suffering from depression after stroke peaks during 3-6 months post-stroke, with most patients achieving remission within 1 year[8]. According to a meta-analysis, the prevalence of depression in post stroke survivors in India is approximately 55%[9]. Studies have shown that patients with left hemisphere damage are at a higher risk of developing depressive symptoms as compared to those with right hemisphere damage. A specific correlation has been determined between presence of lesions in the left anterior frontal lobe or basal ganglia region and post-stroke depression(PSD)[10]. Another neuroimaging study has demonstrated the association of post-stroke depression with lesions in the frontal region, basal ganglia and hippocampus[11]. As the development of post stroke depression has been associated with poor functional outcome and rehabilitation and increased risk of mortality, early recognition and intervention is required. In this study, we aimed to assess the frequency of depression in stroke patients and to study the association between lesion characteristics and post stroke depression.

MATERIALS AND METHODS

The study was approved by the Institutional Ethics Committee of Sri Aurobindo Medical College and Postgraduate Institute, Indore, M.P.

Patients who were referred from the Department of Neurology to the Psychiatry Out-patient Department were assessed. Those with a history of onset of cerebrovascular accident (>2 weeks but <1 year) were interviewed and sociodemographic data and clinical variables were collected using a semi-structured proforma. The type and location of cerebrovascular lesion was assessed using Magnetic Resonance Imaging 1.5 T. The type of stroke was classified as ischaemic or hemorrhagic. The location and extent of lesion was assessed on the basis of laterality (i.e. lesion in left, right or bilateral hemispheres), lobe involvement (frontal, temporal, parietal and occipital lobe) and focal or multilobar involvement. Patients were divided into 2 groups on the basis of duration after onset of stroke as those with time after onset of stroke between 2 weeks to 3 months and those with time after onset of stroke between 3 months to 1 year.

Patients who were unconscious, aphasic, had severe cognitive impairment or were unable to communicate and cooperate with the clinical interview were excluded from the study. Patients with a previous history of stroke, a history of major psychiatric or medical illness affecting their ability to carry out activities of daily living and those who were unable or unwilling to give informed consent were excluded from the study. Those who had a history of stroke in the brainstem area were also excluded from the study.

The presence of Major Depressive Disorder was assessed using DSM-5-TR criteria and the severity was assessed using the Hamilton Depression Rating Scale (HDRS). Patients were also assessed for the level of independence in activities of daily living using the Barthel Index (BI). Patients were divided into 2 groups on the basis of Barthel score as those with a score <65 indicating functional dependence and those with a score of >65 indicating functional independence.

Statistical Analysis: Descriptive statistics were used to summarise socio-demographic and clinical variables. The demographic details, clinical variables and lesion characteristics of stroke patients with depression were compared with those without depression and the association was measured using the Chi-square/Fisher test. For statistically significant association, p value was$\leq$0.05.

RESULTS AND DISCUSSIONS

A total of 44 stroke patients were included in the study. The mean age of the patients included in the study was 61 years±10.8 with 18(40.9%) females and 26(59.1%) males. The association of age, gender, marital status, socioeconomic status, educational status, type of family and residence with depression was not found to be statistically significant. (Table 1)

Out of 44 patients, 27(61.4%) were found to be suffering from depression, while 17(38.6%) did not

Table 1: Sociodemographic variables

Gender		**N (%)**
	Female	18 (40.9)
	Male	26 (59.1)
	Total	44 (100)
Marital status		N (%)
	Married	37 (84.1)
	Widowed	7 (15.9)
	Total	44 (100)
Education		N (%)
	Post graduation	4 (9.1)
	Higher secondary	5 (11.4)
	Secondary	14 (31.8)
	Primary	21 (47.7)
	Total	44 (100)
Family type		N (%)
	Nuclear	34 (77.3)
	Extended nuclear / joint	10 (22.7)
	Total	44 (100)
Residence		N (%)
	Rural	5 (11.4)
	Semi-urban	19 (43.2)
	Urban	20 (45.5)
	Total	44 (100)
Socioeconomic status		N (%)
	Lower	0 (0)
	Upper lower	10 (22.7)
	Lower middle	26 (59.1)
	Upper middle	6 (13.6)
	Upper	2 (4.5)
	Total	44 (100)

Table 2: Frequency and severity of Depression

Depression		**N (%)**
	Present	27 (61.4)
	Absent	17 (38.6)
	Total	44 (100)
Severity of depression		N (%)
	Mild	8 (29.6)
	Moderate	12 (44.4)
	Severe	5 (18.5)
	Very severe	2 (7.5)
	Total	27 (100)

Table 3: Lesion type and depression

Depression				**Total N=44 (%)**	**p-value**
		Absent N= 17(%)	Present N=27 (%)		
Lesion type	Haemorrhagic	4 (33)	8 (66)	12 (27.3)	0.6
	Ischaemic	13 (41)	19 (59)	32 (72.7)	

Table 4: Association of lesion characteristics and Depression

Lesion characteristics	**Depression**			**Total N=44 (%)**	**p-value**
	Absent N= 17(%)	Present N=27 (%)			
Focal /Multi-lobar	Focal	9 (56)	7 (44)	16 (36.4)	0.1
	Multi-lobar	10 (36)	18 (64)	28 (63.6)	
Lesion Laterality	Bilateral	1 (50)	1 (50)	2 (4.5)	0.037
	Left hemisphere	6 (23)	20 (77)	26 (59.1)	
	Right hemisphere	10 (62)	6 (38)	16 (36.4)	
Frontal Lesion location	Absent	11 (58)	8 (42)	19 (43.2)	0.02
	Present	6 (24)	19 (76)	25 (56.8)	
Temporal Lesion location	Absent	10 (37)	17 (63)	27 (61.4)	0.7
	Present	7 (41)	10 (59)	17 (38.6)	
Parietal Lesion location	Absent	6 (40)	9 (60)	15 (34.1)	0.8
	Present	11 (38)	18 (62)	29 (65.9)	
Occipital Lesion location	Absent	15 (68)	22 (32)	37 (84.1)	0.5
	Present	2 (28)	5 (72)	7 (15.9)	
Basal ganglia Lesion	Absent	17 (41)	24 (59)	41 (93.2)	0.15
	Present	0 (0)	3 (100)	3 (6.8)	

Table 5: Clinical variables and Depression

Clinical variables		**Depression**		**Total N=44 (%)**	**p value**
		Absent N=17 (%)	Present N=27 (%)		
Hypertension	Absent	6 (46.1)	7 (53.8)	13 (29.5)	0.50
	Present	11 (35.5)	20 (64.5)	31 (70.5)	
Diabetes Mellitus	Absent	10 (58.9)	7 (41.1)	17 (38.6)	0.03
	Present	7 (26)	20 (74)	27 (61.4)	
Substance dependence	Alcohol	2(25)	6 (75)	8 (18.2)	0.04
	Tobacco	2 (16.7)	10 (83.3)	12 (27.3)	
	Alcohol + tobacco	2 (28.6)	5 (71.4)	7 (15.9)	
	None	11 (64.7)	6 (35.3)	17 (38.6)	

Table 6: Duration after onset of stroke and Depression

Depression				Total N=44 (%)	p-value
		Absent N=17 (%)	Present N=27 (%)		
Duration after onset of stroke	> 2 weeks-< 3 months	7 (28)	18 (72)	25 (56.8)	0.17
	3 months-< 1 year	10 (52.6)	9 (47.4)	19 (43.2)	

Table 7 : Association of Barthel Index and depression

Depression				Total N=44 (%)	p-value
		Absent N=17 (%)	Present N=27(%)		
Barthel Index	Functionally dependent (score <65)	3 (27.31)	8 (72.7)	11 (25)	0.3
	Functionally independent (score >65)	14 (42.4)	19 (57.6)	33 (75)	

have depression. On scoring for severity of depression using the HDRS, 8(29.6%) were found to be suffering from mild depression, 12(44.4%) from moderate depression, 5(18.5%) from severe and 2(7.5%) from very severe depression. (Table 2)

Of the 44 patients, 32(72.7%) had a history of ischaemic stroke and 12(27.3%) had a history of hemorrhagic stroke. Among the 32 patients of ischaemic stroke, 19(59.4%) had depression, while 13(40.6%) did not have depression. Among 12 patients of hemorrhagic stroke, 8(66.7%) had depression while 4(33.3%) did not have depression. The association between type of stroke and depression was not found to be statistically significant (p value >0.05). (Table 3)

Of the 44 patients, 8(18.2%) had a history of alcohol dependence, 12(27.3%) had tobacco dependence and 7(15.9%) had a history of dependence of both alcohol and tobacco. Out of 27 patients with a history of substance dependence, 21(77.8%) of them had depression, while 6(22.2%) did not. This concluded that the association between post-stroke depression and substance dependence was found to be statistically significant (p<0.05).

Among 31 patients with one of the medical comorbidities as hypertension, 20(64.5%) of them had depression, while 11(35.5%) did not have depression, making the association statistically insignificant (p>0.05). Out of 27 patients with Diabetes Mellitus as one of the medical comorbidities, 20(74%) of them had depression, while 7(26%) did not, which was statistically significant (p<0.05) (Table 4)

Out of 44 patients, 25(56.8%) patients had a duration after onset of stroke of <3 months while 19(43.2%) had a duration after onset of stroke of >3 months to <1 year. The association between duration after onset of stroke and depression was not found to be statistically significant (p>0.05) (Table 5)

Out of 44 patients, 26(59.1%) of them had lesions in the left hemisphere, 16(36.4%) had right hemispheric lesions and 2(4.5%) had lesions in the bilateral hemisphere.

Of the 26 patients with left sided lesions, 20(76.9%) had depression while 6(23.1%) did not have depression. The association between left-sided lesion and depression was found to be statistically significant (p<0.05).

Out of 44 patients, 28(63.6%) had multilobar involvement while 16(36.4%) had a focal lesion in a single lobe. Among 28 with a multilobar lesion, 18 (64.3%) had depression, while 10 (35.7%) did not have depression. And among 16 patients with a focal lesion, 7 (43.75%) of them had depression, while 9 (56.25%) of them did not. The association between the presence of focal or multilobar lesions and depression was not found to be statistically significant (p<0.05).

Out of 44 patients, 25 (56.8%) patients had involvement of the frontal lobe (either focal or multilobar lesion) while 19 (43.2%) had lesions in other areas. Out of 25 with frontal lobe involvement, 19(76%) had a diagnosis of depression, while 6(24%) did not have depression. This association was found to be statistically significant (p<0.05). (Table 6)

Out of 44 patients, 33(75%) of them had functional independence and 11 (25%) of them had functional dependence. Out of 33 patients of functional independence, 19 (57.6%) of them had depression and out of 11 patients with functional dependence, 8 (72.7%) of them had depression. The rates of depression were higher in those with higher dependence in activities of daily living, although the association was not statistically significant.

No statistically significant association was found between scoring on Barthel Index and other clinical variables. (Table 7)

This study aimed to identify the frequency and severity of depression in patients with a history of cerebrovascular accident >2 weeks to <1 year prior. Among 44 patients with a history of cerebrovascular stroke, 61.4% of them were diagnosed with depression. This aligns with the data from previous studies which determined that the prevalence rates of post-stroke depression ranging from 18%-61%[12]. A metaanalysis by Hackett M.L. and Pickles K. concluded that the prevalence of post stroke depression was 28% at 1 month after stroke and 31% at any time up to 5 years following stroke[12]. In a study done by Saxena A. and Suman A. the frequency of depression in post stroke patients in a rural tertiary care hospital in India, was found to be 57%[13]. A systematic review and meta-analysis by Patra A. *et al.* reported that the prevalence of post-stroke depression in India was approximately 55%[14].

The frequency of depression in this study is higher than the previously reported data and can be attributed to difference in demography and the assessment of patients after a duration of 2 weeks post-stroke, leading to a higher level of acute stress and reporting of depressive symptoms.

Among 27 patients with depression, 74% of the depressed patients had mild and moderate intensity of depression as measured on the Hamilton Depression Rating Scale (HDRS). This is in keeping with previous studies that have shown a higher incidence of mild to moderate intensity of depression than severe depression in the post-stroke period[14,15].

Among patients with dependence on alcohol, tobacco or both, 77.8% of them had depression. This finding is in alignment with previous studies. Alcohol and tobacco use have been identified as significant risk factors for the development of post-stroke depression[15,16]. Additionally, smoking has been identified as an independent risk factor for causing both stroke and depression[17]. Alcohol also increases the risk of major cardiovascular disorders, including hypertension, ischaemic heart disease and stroke[18]. Alcohol use disorder also has a bidirectional relationship with depression, as alcohol use can cause depression due to long-term neurobiological and metabolic changes and depression in turn can increase the use of alcohol[19].

Among 27 patients with a history of Diabetes Mellitus, 75% of them were found to have depression, making the association statistically significant. This finding was in alignment with previous studies. A systematic review on post-stroke depression found that diabetes mellitus was more commonly reported in PSD patients[22].

In this study, no significant association was found between hypertension and post-stroke depression. Contrasting evidence was found in other studies where hypertension being a vascular risk factor for stroke and an independent risk factor for depression, has been found to be associated with the development of post-stroke depression[22,23].

No association was found between the type of stroke (i.e. ischemic or hemorrhagic) and depression in this study. This finding is similar to that reported by previous data[24,25]. A systematic review and metaanalysis of Imaging markers of Post-stroke depression and apathy also concluded that no significant association was present between lesion type and post-stroke depression[25].

On assessing the association between depression and lesion laterality, this study found that out of all patients with a left hemisphere lesion, 76.9% of them had depression. The study observed that the rate of depression was higher in those with left sided stroke as compared to right-sided stroke patients. This finding is in keeping with data from prior studies. A metaanalysis by Mitchell *et. al.* concluded that the risk of developing depression after stroke is higher in those with left hemisphere stroke[26].

A review on post stroke depression found a positive association between depression and left sided frontal lobe and basal ganglia lesions[18]. A meta-analysis concluded that patients with left hemispheric lesions were more vulnerable to post-stroke depression in the first 6 months after stroke onset[27].

Although many other studies have not shown an association between laterality of lesion and post-stroke depression[5,28], while some others have found an association between right sided cerebrovascular lesion and depression[29,30].

The presence of conflicting evidence in this area can be explained by the difference due to the assessment of patients in acute and chronic phase after stroke onset.

This study observed that patients with involvement of the frontal lobe in either focal or multilobar lesions reported higher rates of post-stroke depression. Development of post-stroke depression can be explained on the basis of neurobiology as disturbances in biogenic amine functioning and ischaemic or inflammatory damage to structures in the frontal lobe can cause depressive symptoms[5].

A study by Robinson R. G. and Jorge R. E. observed that poststroke depression was more commonly seen in those with frontal lobe and basal ganglia lesions[22]. A study reported that ischaemic damage to the frontal subcortical areas was significantly associated with the development of post-stroke depression[31].

Higher odds of post-stroke depression were observed in patients with a frontal lobe lesion in a meta-analysis of markers of post-stroke depression[21]. Some studies have reported no association between anatomical location of cerebrovascular lesion and post-stroke depression[32,33]. A study analysing depressive symptoms 2 years after the onset of stroke found no association between lesion location and post-stroke depression[28]. This study found that all the patients with basal ganglia lesion had developed post stroke depression but due to the small sample(3 patients), a significant association could not be determined.

This study observed that 72.2% of the patients with functional dependence in activities of daily living (ADLs) were depressed and 57.6% of the patients with functional independence were depressed. This concludes that the rate of depression is higher in those with more dependence in ADLs, although not statistically significant. Previous studies have shown

that there is a significant association between post-stroke depression and functional independence in carrying out activities of daily living (ADLs). A bidirectional relationship between post-stroke depression and deficits in ADLs has been suggested. Patients with poorer functioning and higher dependence in ADLs have shown a higher rate of post-stroke depression[4,34]. The development of post-stroke depression increases the risk of functional deficit and a higher severity of depression has been found to be an independent predictor of functional impairment 1 or more years after stroke[22]. A prospective study by Baccaro *et al.* concluded that higher functional disability in post-stroke patients has been associated with the presence of depression at 6 months and 2 years after stroke onset[28]. A study by Rajashekaran P. *et al.* found a significant correlation between lower scores on Barthel Index and rates of post-stroke depression[35].

CONCLUSION

Post-stroke depression (PSD) is one of the most prevalent neuropsychiatric manifestations of cerebrovascular injury affecting nearly one in every three patients with a history of stroke. Common medical comorbidities like hypertension and diabetes mellitus act as risk factors for both stroke and depression. Presence of PSD negatively impacts the lives of stroke survivors and their caregivers[36]. In this study, 61.4% patients were diagnosed with post-stroke depression(PSD), with mild to moderate intensity being more commonly seen. PSD was found to be significantly higher in patients with a left hemispheric lesion and involvement of the frontal cortex. However, lesion size did not show any significant difference in post-stroke depression. History of substance use was associated with an increase in the frequency of depression in post-stroke patients. Presence of Diabetes Mellitus was also associated with PSD. As PSD is underrecognized and undertreated, assessing post-stroke patients for depression is required to improve rehabilitative and functional outcomes. This would also help in identification of patients who are at a higher risk of developing PSD and providing early intervention for the same.

Limitations: The present study was conducted in a tertiary care hospital, using convenience sampling and a small sample size, therefore the results of this study cannot be generalised for the community. Our sample represents patients who had lesser functional disability and showed lower severity of post-stroke depression, due to which the results cannot be applied to patients with higher stroke severity and functional disability. Other vascular medical comorbidities like ischaemic heart disease, which can increase the risk of both stroke and depression independently, were not taken into consideration.

REFERENCES

1. Sacco, R.L., S.E. Kasner, J.P. Broderick, L.R. Caplan and J.J. (Buddy) Connors et al., 2013. An updated definition of stroke for the 21st century. Stroke, 44: 2064-2089.
2. First, M.D. and B. Michael, 2024. DSM-5-TR® Handbook of Differential Diagnosis. Amer Psychiatric Pub Inc, Washington, ISBN-14: 978-1615373598, Pages: 372.
3. Jaroonpipatkul, C., J. Onwanna, C. Tunvirachaisakul, N. Jittapiromsak and Y. Rakvongthai et al., 2022. Depressive symptoms due to stroke are strongly predicted by the volume and location of the cerebral infarction, white matter hyperintensities, hypertension, and age: A precision nomothetic psychiatry analysis. J. Affe Disord., 309: 141-150.
4. Srivastava, A., A. Taly, A. Gupta and T. Murali, 2010. Post-stroke depression: Prevalence and relationship with disability in chronic stroke survivors. Ann. Indi Acad. Neurol., 13: 123-127.
5. Pedroso, V.S.P., L.C. Souza, A.R. Brunoni and A.L. Teixeira, 2015. Post stroke depression: Clinics, etiopathogenesis and therapeutics. Arch. Clin. Psy São Paulo., 42: 18-24.
6. Towfighi, A., B. Ovbiagele, N.E. Husseini, M.L. Hackett and R.E. Jorge et al., 2017. Poststroke depression: A scientific statement for healthcare professionals from the American heart association/american stroke association. Stroke, 48: 30-43.
7. Ayerbe, L., S. Ayis, C.D.A. Wolfe and A.G. Rudd, 2013. Natural history, predictors and outcomes of depression after stroke: Systematic review and meta-analysis. Br. J. Psy., 202: 14-21.
8. Ayerbe, L., S. Ayis, S. Crichton, C.D.A. Wolfe and A.G. Rudd, 2013. The long-term outcomes of depression up to 10 years after stroke; the south london stroke register. J. Neu. Neu. amp Psy., 85: 514-521.
9. Patra, A., K. Nitin, N.M. Devi, S. Surya and M.G. Lewis,et al., 2021. Prevalence of depression among stroke survivors in India: a systematic review and meta-analysis. Fron neur neu res., Vol. 2.
10. Singh, A., S.E. Black, N. Herrmann, F.S. Leibovitch and P.L. Ebert,et al., 2000. Functional and neuroanatomic correlations in poststroke depression. Stroke, 31: 637-644.
11. Taylor, W.D., H.J. Aizenstein and G.S. Alexopoulos, 2013. The vascular depression hypothesis: Mechanisms linking vascular disease with depression. Mol. Psyc., 18: 963-974.

12. Hackett, M.L. and K. Pickles, 2014. Part i: Frequency of depression after stroke: An updated systematic review and meta-analysis of observational studies. Int. J. Stroke, 9: 1017-1025.
13. Saxena, A. and A. Suman, 2015. Magnitude and determinants of depression in acute stroke patients admitted in a rural tertiary care hospital. J. Neu Rural Pract., 6: 202-207.
14. Liu, L., I.J. Marshall, R. Pei, A. Bhalla, C.D. Wolfe, M.D. O'Connell and Y. Wang, 2024. Natural history of depression up to 18 years after stroke: A population-based south london stroke register study. Lan Reg Hea Eur., Vol. 40 .10.1016/j.lanepe.2024.100882.
15. Qawasmeh, M.A., B. Aldabbour, A. Abuabada, K. Abdelrahman and S. Elamassie et al., 2022. Prevalence, severity, and predictors of poststroke depression in a prospective cohort of Jordanian patients. Stroke Res. Treat., 2022: 1-10.
16. Rabat, Y., I. Sibon and S. Berthoz, 2021. Implication of problematic substance use in poststroke depression: An hospital-based study. Sci. Rep., Vol. 11 .10.1038/s41598-021-92639-5.
17. Fluharty, M., A.E. Taylor, M. Grabski and M.R. Munafò, 2016. The association of cigarette smoking with depression and anxiety: A systematic review. Nic amp Tob Res., 19: 3-13.
18. Roerecke, M., 2021. Alcohol's impact on the cardiovascular system. Nutrients, Vol. 13, No. 10 .10.3390/nu13103419.
19. Boden, J.M. and D.M. Fergusson, 2011. Alcohol and depression. Addiction., 106: 906-914.
20. Aben, I., J. Denollet, R. Lousberg, F. Verhey, F. Wojciechowski and A. Honig, 2002. Personality and vulnerability to depression in stroke patients. Stroke, 33: 2391-2395.
21. Shi, Y., D. Yang, Y. Zeng and W. Wu, 2017. Risk factors for post-stroke depression: A meta-analysis. Front. Aging Neu., Vol. 9 .10.3389/fnagi.2017.00218.
22. Robinson, R.G. and R.E. Jorge, 2016. Post-stroke depression: A review. Am. J. Psyc., 173: 221-231.
23. Tennen, G., N. Herrmann, S.E. Black, K.S. Levy, J. Cappell, A. Li and K.L. Lanctôt, 2011. Are vascular risk factors associated with post-stroke depressive symptoms? J. Ger Psy Neurol., 24: 215-221.
24. Isuru, A., A. Hapangama, D. Ediriweera, L. Samarasinghe and M. Fonseka,et al., 2021. Prevalence and predictors of new onset depression in the acute phase of stroke. Asian J. Psy., Vol. 59 .10.1016/j.ajp.2021.102636.
25. Douven, E., S. Köhler, M.M.F. Rodriguez, J. Staals, F.R.J. Verhey and P. Aalten, 2017. Imaging markers of post-stroke depression and apathy: A systematic review and meta-analysis. Neu Rev., 27: 202-219.
26. Mitchell, A.J., B. Sheth, J. Gill, M. Yadegarfar and B. Stubbs,et al., 2017. Prevalence and predictors of post-stroke mood disorders: A meta-analysis and meta-regression of depression, anxiety and adjustment disorder. Gen. Hosp. Psy., 47: 48-60.
27. Zhang, Y., H. Zhao, Y. Fang, S. Wang and H. Zhou, 2017. The association between lesion location, sex and poststroke depression: Meta-analysis. Brain Behav., Vol. 7, No. 10 .10.1002/brb3.788.
28. Baccaro, A., Y.P. Wang, A.R. Brunoni, M. Candido and A.B. Conforto et al., 2019. Does stroke laterality predict major depression and cognitive impairment after stroke? two-year prospective evaluation in the emma study. Prog. Neu Psy Bio. Psy., Vol. 94 .10.1016/j.pnpbp.2019.109639.
29. Yu, L., C. Liu, J. Chen, S. Wang, Y. Wu and S. Yu, 2004. Relationship between post-stroke depression and lesion location: A meta-analysis. Kao J. Med. Sci., 20: 372-380.
30. Metoki, N., N. Sugawara, J. Hagii, S. Saito and H. Shiroto et al., 2016. Relationship between the lesion location of acute ischemic stroke and early depressive symptoms in Japanese patients. Ann. Gen. Psy., 15: 1-6.
31. Tang, W.K., J.Y. Lu, Y.K. Chen, W.C.W. Chu and V. Mok,et al., 2010. Association of frontal subcortical circuits infarcts in poststroke depression: A magnetic resonance imaging study of 591 Chinese patients with ischemic stroke. J. Ge Psy Neurol., 24: 44-49.
32. Carson, A.J., S. MacHale, K. Allen, S.M. Lawrie and M. Dennis,et al., 2000. Depression after stroke and lesion location: A systematic review. Lancet, 356: 122-126.
33. Kotsa, K., M.P. Yavropoulou, O. Anastasiou and J.G. Yovos, 2009. Role of vitamin D treatment in glucose metabolism in polycystic ovary syndrome. Fertil. Sterility, 92: 1053-1058.
34. Robinson, R.G., 2006. The Clinical Neuropsychiatry of stroke: Cognitive, Behavioral and Emotional Disorders Following Vascular Brain Injury.Cambridge University Press.
35. Rajashekaran, P., K. Pai, R. Thunga and B. Unnikrishnan, 2013. Post-stroke depression and lesion location: A hospital based cross-sectional study. Indian J. Psy., 55: 343-348.
36. Das, J. and R.G. K, 2018. Post stroke depression: The sequelae of cerebral stroke. Neu. amp Biob Rev., 90: 104-114.