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The Prevalence and Predictors of Post-Stroke Depression and Anxiety During COVID-19 Pandemic

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Introduction: Stroke is associated with a rise in post-stroke depression (PSD) and anxiety (PSA). In this study, we evaluated the impact of COVID-19 pandemic on the rates of PSD and PSA. *Methods:* All stroke admissions to two hospitals in Saudi Arabia during two months were prospectively evaluated for PSD and PSA. NIHSS and serum TSH assessed on admission. PSD and PSA were evaluated using Hospital Anxiety and Depression Scale (HADS). Post-stroke disability was assessed by mRS, while social support assessed by Multidimensional Scale of Perceived Social Support (MSPSS). *Results:* Among 50 participants (28 males), clinically significant PSD was found in 36%, while PSA in 32%. PSD associated with higher NIHSS ($P < 0.001$); lower MSPSS ($P = 0.003$); higher mRS ($P = 0.001$); and discontinuation of rehabilitation ($P = 0.02$). PSA was associated with higher TSH ($P = 0.01$); lower MSPSS ($P = 0.03$); while discontinuation of rehabilitation was related to less PSA ($P = 0.034$). Multivariate analysis showed that NIHSS (OR: 1.58, 95% CI: 742−3.37; $P = 0.01$); and MSPSS score (OR: 0.66, 95% CI: 0.47−0.94; $P = 0.002$) were associated with PSD; while PSA was related to TSH level (OR: 8.32, 95% CI:1.42−47.23; $P = 0.02$), and discontinuation of rehabilitation (OR: -0.96, 95% CI: -1.90−0.02; $P = 0.04$). *Conclusions:* Our research shows that the rise in PSD is related to stroke severity and this has not changed significantly during the pandemic; however, PSA showed a noticeable peak. Social deprivation and the lacking levels of rehabilitation related significantly to both.

Key Words: COVID-19—Ischemic stroke—Depression—Anxiety—Social support

Introduction

Mood and anxiety disorders are common amongst hospitalized patients with life-threating illnesses or chronic ailments. This may have an impact on the prognosis of certain conditions and patients' quality of life.[1,2] Moreover, the social isolation of hospitalized patients, which is mandatory during pandemics, has been linked to a worse mental health outcome and emotional distress.[3] The novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has recently been declared a pandemic and have a severe psychological influence on the mental health of healthcare workers as well as hospitalized patients.[4,5]

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Post-stroke depression (PSD) and post-stroke anxiety (PSA) are common among stroke patients.[6] Clinically, about 30% of stroke survivors have PSD symptoms during acute stage, while PSA prevalence following a stroke is estimated to be between 20% and 25%.[7,8] Acute PSD was present in a fifth of stroke patients in a recent study from the Middle East, with higher rates in women compared to men.[9] Furthermore, over a half of stroke patients will experience either PSD or PSA at some point, resulting in an obvious impact on neurological and functional deficits.[10] Stroke patients who underwent intensive and regular rehabilitations showed an improvement in both physical and mental health; hence, a change in depression scores may be noticed.[11]

There are no studies on the mental health of hospitalized stroke patients during the new coronavirus disease 2019 (COVID-19) outbreak. There are certainly some limitations when it comes to visiting family members at hospitals during this pandemic with unknown consequences on PSD or PSA. Furthermore, access to regular and efficient rehabilitation services may also be limited during the pandemic, leading to a further increased risk in PSD and PSA. Hence, it is crucial to investigate the rates of depression and anxiety in stroke patients during COVID-19 pandemic.

In the present study, we aimed to explore the prevalence and factors linked to PSD and PSA among stroke patients hospitalized during the early phase of COVID-19 pandemic in Saudi Arabia. The results may alert healthcare workers to provide early psychological interventions to improve mental and physical health of stroke patients.

Patients and Methods

Patients

During this study, we investigated all patients, with a clinical and a radiological evidence of acute ischemic stroke, who were admitted to two tertiary stroke centers, Saudi German Hospital in Madinah and Jeddah in Kingdom of Saudi Arabia, during the period from 1st of February - 31st of March 2020. Patients with acute stroke, who in addition had any of the following features were excluded: (1) fever, cough or any acute respiratory symptoms; (2) any chronic psychiatric or neurocognitive disorder obtained during patients interview or from their medical records; (3) pre-existing chronic neurological disorders, especially stroke with a residual disability; (4) patients with chronic debilitating medical disorders such as, chronic renal failure, heart failure, neoplastic disorders, thyroid or other endocrinal disorders were also excluded. Prior to enrollment into the study, written informed consents were obtained from all patients or relatives. Additionally, The Ethics Committee of Saudi German hospital group approved this study.

Measures

All patients were assessed for: (1) stroke severity at the time of admission with National Institute of Health Stroke Scale (NIHSS)[12]; (2) routine blood investigations, including serum levels of thyroid stimulating hormone (TSH) at the time of admission, and this was categorized as low $>$ 0.4, normal 0.4−4, or high $>$ 4. (3) Cognitive state, using mini-mental state examination (MMSE).[13] During period of hospitalization, medical escorts or visitors for all patients were prohibited, following the regulations of Ministry of health (MOH) to prevent infection spread.[14] Stroke subtypes were classified according to TOAST classification, using various imaging and clinical data.[15] Follow-up at 90 days was conducted in outpatient clinics or via telemedicine communication. Social support during hospitalization and three months following discharge was assessed using self-reported Multidimensional Scale of Perceived Social Support (MSPSS).[16] PSD and PSA were also assessed using Hospital Anxiety and Depression Scale (HADS).[17] In addition, Modified Rankin Scale (mRS) was used to evaluate Post-stroke disability after 3 months.[18]

Statistical Analysis

We used the IBM SPSS software package version 20.0 for data analysis. (Armonk, NY: IBM Corp). Qualitative data was described using numbers and percentage points. Quantitative data was described using a range (minimum and maximum), a mean, or a standard deviation, a median and an interquartile range (IQR). Chi-square test was used for categorical variables, to compare between different categories. Student t-test was used for normally distributed quantitative variables, to compare between two studied categories, while Mann Whitney test was used for abnormally distributed quantitative variables. A regression analysis was also used to detect the most independent/affecting factor for assessing post-stroke depression and anxiety. The significance of the obtained results was judged at confidence interval (CI) set to 95% and the margin of error accepted was set to 5%, and a $P < 0.05$ was considered statistically significant.

Results

Sociodemographic and clinical characteristics

We identified 68 patients eligible for enrolment in our study during the two months of the study period with acute stroke. We excluded 16 patients due to cognitive dysfunctions (MMSE $<$ 25), or due to significant stroke deficit that may affect their participation in the study (Severe speech disorders, visual difficulties, or memory affection).

A total of 52 participants, including 28 males and 24 females were included in current study. Half the patients where Saudi Nationals and the remainder of patients were from South-East Asia and surrounding Middle Eastern countries. Following discharge from hospital, 3-month assessment was possible in 50 subjects. All participants were

Table 1. *Sociodemographic and clinical characteristics of patients with acute ischemic stroke (n = 50).*

	Mean (SD)	Range
Demographic data		
Age (years)	56.72 ± 11.83	29–75
Gender Male	28 (56%)	
Gender Female	22 (44%)	
NIHSS score at time of admission	7.60 ± 3.92	2–18
TSH level at time of admission	2.48 ± 2.61	0.10–9
Low (<0.4)	16 (32%)	
Normal (0.4–4)	25 (50%)	
High (>4)	9 (18%)	
TOAST Classification		
Large vessel atherosclerosis	14 (28%)	
Small vessel occlusion	10 (20%)	
Cardio-embolic source	9 (18%)	
Others etiologies	11 (22%)	
Undetermined etiologies	6 (12%)	
MMSE	26.64 ± 1.37	25–29
mRS after 3 months	1.64 ± 1.19	0–5
Discontinuation of rehabilitation		
Yes	27 (54%)	
No	23 (46%)	
Social support using MSPSS	5.40 ± 1.17	2.0–11
Post stroke depression using HADS-D	6.35 ± 4.03	0–16
No depression	32 (64%)	
Mild Depression	5 (10%)	
Moderate Depression	7 (14%)	
Severe Depression	6 (12%)	
Post stroke anxiety using HADS-A	9.01 ± 4.24	0–21
No Anxiety	36 (72%)	
Mild Anxiety	6 (12%)	
Moderate Anxiety	7 (14%)	
Severe Anxiety	3 (6%)	

Note. NIHSS=Neurological Institute of Health Stroke Scale; TSH=Thyroid Stimulating Hormone; MMSE=Mini Mental State Examination; mRS=Modified Rankin Scale; MSPSS=Multidimensional Scale of Perceived Social Support; HADS=Hospital Anxiety and Depression Scale.

age and sex matched. The participants' demographic, clinical, MSPSS and HADS scores are given in Table 1.

Psychosocial characteristics of the participants

The mean depression subscale (HADS-D) and anxiety subscale (HADS-A) scores were 6.57 ± 4.16 and 5.24 ± 4.21, respectively. With reference to HADS, depression and anxiety symptoms were present in 18 (36%) and 16 (32%) participants respectively. Depression was mild in 5 (10%), moderate in 7 (14%), and severe in 6 (12%) patients. Anxiety levels were mild, moderate and severe in 6 (12%), 7 (14%) and 3 (6%) patients respectively.

Factors associated with depression and anxiety among patients

In order to investigate the factors related to depression and anxiety among stroke patients, HADS-D score results were compared between depressed and non-depressed patient's different parameters (Table 2). We also used HADS-A score results to compare between anxiety and non-anxiety patients testing different parameters (Table 3). As shown in Table 2, depression scores were significantly higher in patients with higher NIHSS score (mean 11.11 ± 3.89 with $P < 0.001$); lower TSH levels at admission (mean 1.04 ± 1.23 with $P = 0.03$); mRS at 3 months (mean 2.67 ± 1.03 with $P < 0.001$); lower social support (mean 4.53 ± 3.89 with $P = 0.001$); and discontinuation of rehabilitation, with $P < 0.001$.

Anxiety scores were significantly higher in patients with higher TSH levels at admission (mean 3.96 ± 3.09 with $P = 0.006$); lower social support (mean 5.89 ± 4.28 with $P = 0.009$); and discontinuation of rehabilitation, with $P = 0.02$ as shown in Table 3.

Univariate and multivariate analysis of different parameters influencing PSD and PSA

Univariate and multivariate analysis were used for detection of parameters' highly influencing (independent risk factors) both PSD and PSA. We investigated the effects of NIHSS, MSPSS and mRS at 3 months on PSD (see Table 4). The results showed that NIHSS at admission (odds ratio (OR): 1.80, 95% confidence interval (CI):1.299–2.48); MSPSS score (OR: 0.44, 95% CI: 0.26–0.75); mRS at 3 months (OR: 9.38, 95% CI: 2.39–36.7); and discontinuation of rehabilitation (OR: 5.25, 95% CI: 1.92–8.57) were the univariates parameters significantly influencing PSD ($P < 0.001$, 0.003, 0.001, and 0.02 respectively). Moreover, multivariate analysis of these factors (Table 4) showed that NIHSS (OR: 1.58, 95% CI: 742–3.37); MSPSS score (OR: 0.66, 95% CI: 0.47–0.94) were multivariate parameters that significantly influenced PSD ($P = 0.01$, and 0.002, respectively). mRS at 3 months (OR: 7.425, 95% CI: 0.341–161.8) and discontinuation of rehabilitation (OR: 3.75, 95% CI: 0.61–6.88) were not statistically significant ($P = 0.202$, and 0.059, respectively).

Parameters' that were significantly higher in PSA on univariate analysis included high TSH at admission (OR: 9.54, 95% CI: 1.71–53.12), MSPSS (OR: 0.65, 95% CI: 0.39–1.47) and discontinuation of rehabilitation (OR: -1.28, 95% CI: -2.22–-0.35), with significant statistically analysis ($P = 0.01$, 0.03, and 0.034 respectively). Multivariate analysis showed that high TSH level during admission (OR: 8.32, 95% CI:1.42–47.23) and discontinuation of rehabilitation (OR: -0.96, 95% CI: -1.90–-0.02) were associated with PSA ($P = 0.02$, and 0.04, respectively); while MSPSS score (OR: 0.85, 95% CI: 0.59–1.20) was not statistically significant between patients with or without PSA ($P = 0.15$). The severity of stroke symptoms (as measured on NIHSS), and post-stroke disability did not seem to effect PSA.

Table 2. *Comparison of different parameters among depressed and non-depressed stroke patients (n = 50).*

	No depression (n = 32)	Depression (n = 18)	p value
Age (years)			
Min.−Max.	29.0−75.0	30.0−75.0	0.825*
Mean ± SD.	56.44 ± 12.50	57.22 ± 10.87	
Gender			
Male	19 (59.4%)	9 (50%)	0.522**
Female	13 (40.6%)	9 (50%)	
NIHSS at admission			
Min.−Max.	2.0−11.0	5.0 ± 18.0	<0.001***
Mean ± SD.	5.63. ± 2.18	11.11 ± 3.89	
TSH level at admission			
Min. ± Max.	0.10−9.0	0.10−3.0	0.03**
Mean ± SD.	3.28 ± 2.83	1.04 ± 1.23	
TOAST Classification			
Large vessel atherosclerosis	7 (15.6%)	7 (38.8%)	0.364**
Small vessel occlusion	6 (18.8%)	4 (22.2%)	
Cardio-embolic source	3 (9.3%)	6 (33.3%)	
Others etiologies	6 (18.8%)	5 (27.8%)	
Undetermined etiologies	2 (6.2%)	4 (22.2%)	
Discontinuation of rehabilitation			
Yes	14 (43.8%)	13 (72.2 %)	<0.001**
No	18 (56.2%)	5 (27.8%)	
mRS after 3 months			
Min.−Max.	0.0−2.0	1.0−5.0	<0.001***
Mean ± SD.	1.06 ± 0.84	2.67 ± 1.03	
MSPSS Score			
Min.−Max.	3.0−10.0	2.0−8.0	
Mean ± SD.	6.96 ± 4.63	4.53 ± 3.89	0.001***

Note. NIHSS=Neurological Institute of Health Stroke Scale; TSH=Thyroid Stimulating Hormone; mRS=Modified Rankin Scale; MSPSS=Multidimensional Scale of Perceived Social Support.
*Student t-test;
**Chi square test;
***Mann Whitney test.

Discussion

We sought to explore the relationship between the social deprivation and the lack of rehabilitation services with the risk of PSD and PSA in patients admitted with an acute stroke during COVID-19 pandemic. Our main results show that whereas the rates of PSD may be comparable to rates evident during non-pandemic time, PSA was significantly higher during initial months of the pandemic.

The rates of PSD and PSA in stroke patients vary widely across studies.[9,10,19] This may be due in part to the instruments that are used (e.g., structured, semi-structured interview vs. a self-report scale) to examine the patients. The prevalence of PSD from a recent report in our region was approximately 20%,[9] which is comparable to reports conducted in other regions in the world.[10,19] This is somewhat lower than the prevalence in our current study as 36% of patients displaying clinically significant symptoms of depression. The prevalence rate for PSA in our study is 32%, which is higher than what has been reported in one systematic review conducted by Campbell Burton and colleagues (18%),[8] or what was found in another recent study (19.7%).[20]

We found a significant correlation between PSD and a higher NIHSS at the time of admission. Greater stroke severity among hospitalized patients and reduction in stroke admissions during the COVID-19 pandemic have been reported,[21,22] and this has mostly been a result of unwilling of hospital visit by patients with mild symptoms in fear of SARS-CoV-2 infection. Our study also found that a higher mRS and discontinuation of rehabilitation services, among other elective services suspended during COVID-19 outbreak, were associated with more PSD (Table 2). Previous studies have shown the importance of a regular post-stroke rehabilitation, as better 90-days mRS outcome and low rates of PSD were noted.[11,23] An interesting finding in our study was noticing that discontinuation of rehabilitation programs has had a negative relation with PSA. This was likely related to the fear of acquiring SARS-CoV-2 infection during regular hospital visits or stay.[14,21] Furthermore, we were unable to show a

Table 3. *Comparison of different parameters among anxiety and non-anxiety stroke patients (n = 50).*

	No anxiety (n = 34)	Anxiety (n = 16)	p value
Age (years)			
Min. − Max.	30.0−75.0	29.0−74.0	0.494*
Mean ± SD.	57.66 ± 10.71	55.06 ± 13.76	
Gender			
Male	19 (59.4%)	9 (50%)	0.522**
Female	13 (40.6%)	9 (50%)	
NIHSS score at time of admission			
Min. − Max.	2.0−18.0	3.0−11.0	0.959***
Mean ± SD.	7.97 ± 4.70	6.94 ± 1.80	
TSH level at time of admission			
Min. − Max.	0.10−8.0	0.30−9.0	0.006**
Mean ± SD.	1.64 ± 1.87	3.96 ± 3.09	
TOAST Classification			
Large vessel atherosclerosis	9 (25%)	5 (31%)	0.731**
Small vessel occlusion	7 (19.4%)	3 (18.8%)	
Cardio-embolic source	5 (13.8%)	4 (25%)	
Others etiologies	6 (16.6%)	5 (31%)	
Undetermined etiologies	3 (8%)	3 (18.8%)	
Discontinuation of rehabilitation			
Yes	21 (58.3%)	6 (42.9 %)	0.02**
No	15 (41.7%)	8 (57.1%)	
mRS after 3 months			
Min. − Max.	0.0−5.0	0.0−2.0	0.867***
Mean ± SD.	1.69 ± 1.42	1.56 ± 0.62	
MSPSS Score			
Min. − Max.	3.0−11.0	2.0−9.0	0.009***
Mean ± SD.	7.13 ± 4.23	5.89 ± 4.28	

Note. NIHSS=Neurological Institute of Health Stroke Scale; TSH=Thyroid Stimulating Hormone; mRS=Modified Rankin Scale; MSPSS=Multidimensional Scale of Perceived Social Support.
*Student t-test;
**Chi square test;
***Mann Whitney test.

Table 4. *Univariate and multivariate analysis for the parameters influencing post-stroke depression (PSD) and post-stroke anxiety (PSA).*

Post-stroke depression	Univariate		#Multivariate	
	OR (95% C.I)	p value	OR (95% C.I)	p value
NIHSS at admission	1.80 (1.299−2.48)	<0.001	1.58 (0.742−3.37)	0.01
MSPSS Score	0.44 (0.26−0.75)	0.003	0.66 (0.47−0.94)	0.002
mRS after 3 months	9.38 (2.39−36.7)	0.001	7.425 (0.341−161.8)	0.202
Discontinuation of rehabilitation	5.25 (1.92 8.57)	0.02	3.75 (0.61 − 6.88)	0.06
Post-stroke anxiety				
High TSH at admission	9.54 (1.71−53.12)	0.01	8.32 (1.42−47.23)	0.02
MSPSS Score	0.65 (0.39−1.47)	0.03	0.85 (0.59−1.20)	0.15
Discontinuation of rehabilitation	-1.28 (-2.22−-0.35)	0.034	- 0.96 (-1.90−-0.02)	0.04

OR: Odd's ratio, C.I: Confidence interval.
Note. NIHSS=Neurological Institute of Health Stroke Scale; TSH=Thyroid Stimulating Hormone; MSPSS=Multidimensional Scale of Perceived Social Support.
#: All variables with $p < 0.05$ was included in the multivariate.

relation between the severity of symptoms, as measured on the admission by NIHSS or mRS after 3 months, with increasing PSA symptoms.

In line with previous publications,[24−26] we found that lower TSH level at admission was associated with more PSD, whereas higher TSH levels were significantly

associated with PSA. One possible explanation to this could be the fact that depressed TSH serum level will increase basal metabolic rate and neurotoxicity; while, subclinical hyperthyroidism not only increases the risk of anxiety, but also has a direct cardiovascular effect, suggesting that neuroendocrine responses may have a role in post-stroke PSD and PSA.[27,28] Conversely, one recent systematic review by Mitchell and colleagues,[10] did not find direct relation between TSH and PSD or PSA.

In the present study, it is important to note that the social support was a key factor linked to higher PSD and PSA rates (Table 4). Less social support correlated with more depression and anxiety symptoms, along with higher HADS scores (Table 2,3 respectively). We showed that deprivation in patients with ischemic stroke exhibited a worsening of their depression and anxiety symptoms. This was attributed to altered family care and closeness during the outbreak, and this emotional burden was much more pronounced in patients with a respect towards healthcare service. Our results are concurrent with previous reports about social support role in multiple sclerosis patients.[29] Furthermore, two recent reports during COVID-19 outbreak concluded that, the positive role of a perceived social support is associated with low levels of depression and anxiety among other neurological disorders.[30,31]

We recognize the following limitations of this study. First, the size of the study is small. Second, we also did not offer a psychiatric assessment to our patients, which is vital for inclusion, owing to limited healthcare staffing during COVID-19 pandemic. We have also acknowledged the importance of conducting additional large studies from different ethnicities, which would be necessary to predict PSD and PSA and whether early initiation of psychiatric interventions may prevent or improve the quality of life and the functional outcome of stroke patients.

Conclusion

We evaluated if there will be major changes during COVID-19 pandemic on the rates of PSD and PSA in patients presenting with acute stroke symptoms. Our study shows that whilst the rates of depression did not increase significantly; there was, however, a rise in the rates of anxiety in stroke patients during COVID-19 crisis. The higher rates of anxiety during the pandemic are important to recognize and it is likely related to the social deprivation and the lack of rehabilitation services. Early recognition and treatment of this may limit the consequences associated with those disorders.

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