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Original Article

Effect of Sertraline in Newly Diagnosed Depression Patients with Post MI and Stroke: A Prospective Cohort Study

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ABSTRACT

Background: Depression is a condition that affects mental health defined by persistent feelings of sadness and reduced interest in daily activities. Myocardial Infarction (MI) and stroke significantly contribute to global mortality and disability rates. Compared to other antidepressant medications, sertraline demonstrates a lower risk of overdose-related mortality, a reduced potential for dependence, and typically better tolerated by patients. The study focused on evaluating the efficacy of sertraline in managing newly diagnosed depression among patients who have suffered a stroke or MI. **Materials and Methods:** A prospective cohort study includes participants assigned to two groups: Group A (post-MI depression) and Group B (post-stroke depression). We evaluated the severity of depression using HAM-D scores from baseline to Week 24, along with clinical parameters such as lipid profiles, HbA1c, blood pressure, and coagulation factors. We also measured medication adherence using MARS and assessed Health-Related Quality of Life (HRQoL) using RAND-36. **Results:** This research comprised 129 participants, with 62 assigned to group A and 67 to group B. Statistical analysis indicated that sertraline resulted in symptom reduction of depression across both groups, with group B (Post-stroke patients) demonstrating a clinical enhancement in the HAM-D score at week 24. Post-stroke patients showed a more favorable response in TC, HDL, LDL, and TG levels compared to MI patients; Nevertheless, this variation did not achieve significance ($p>0.05$). **Conclusion:** Sertraline effectively reduced depressive symptoms in both groups, with post-stroke patients demonstrating overall improvements in HAM-D scores, lipid profile, medication adherence, and HRQoL.

Keywords: Depression, Stroke, MI, Quality of life, Sertraline.

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INTRODUCTION

Depression is a psychological disorder defined by enduring feelings of sadness and a diminished ability to feel pleasure (Li *et al.*, 2023). Myocardial Infarction (MI) and stroke are major contributors to global mortality and disability, largely due to their shared underlying mechanisms (Gandhi & Kishore, 2020). The pooled data shows that 23% of stroke patients experience depression, while the prevalence is slightly higher at 25.9% for those who have suffered a MI (Aw *et al.*, 2022).

Antidepressants have proven to alleviate depression; their application in individuals with Cardiovascular Disease (CVD) remains a contentious issue. Sertraline is a well-known antidepressant from the SSRI class. It works by increasing serotonin levels in the brain by inhibiting its reabsorption (Padmapriya *et al.*, 2020) Sertraline is particularly notable for its lowers risk of overdose mortality and does not carry the potential for dependency (McRae & Brady, 2001). SSRIs has the ability to stabilize endothelial cells, suppress platelet activity. Nonetheless, the comprehensive clinical significance of these effects remains to be established (O'Connor *et al.*, 2010; Stuckart *et al.*, 2021). Evidence suggests that these agents may facilitate functional recovery following a stroke by modulating ischemia-induced hyper excitation, inflammation, and support the growth of new neurons in the hippocampus. SSRIs were discovered to lower depression levels without having any adverse cardiovascular effects in multiple studies (Gurbel *et al.*, 2002). Despite numerous

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studies highlighting the advantages of sertraline for managing depression in patients with cardiovascular disease and stroke, there are still significant research gaps concerning its safety profile, long-term effects, and potential influence on cardiovascular outcomes (Li *et al.*, 2017; Rasmussen *et al.*, 2003). The aim of the present study was to evaluate the effects of sertraline in treating depression among patients who have experienced a stroke or MI.

MATERIALS AND METHODS

Study design and site

A cohort study was carried out over six months at the outpatient department of Psychiatry in a tertiary care teaching hospital.

Ethical consideration

The SRIHER (DU) Human Institutional Ethics Committee in Chennai, Tamil Nadu, India, approved the research protocol (CSP/19/NOV/81/409). The study followed the updated National Ethical Guidelines for Biomedical and Health Research Involving Human Participants from the Indian Council of Medical Research and all participants gave written informed consent.

Study criteria

Study participants aged 18 to 60 years, regardless of gender, who had experienced a MI or stroke and presented with manifestations of moderate depression during follow-up visits to the psychiatry outpatient department were involved in the study. These individuals were clinically assessed according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition and with Hamilton Depression Rating Scale (HAM-D), taking into account on comorbidities related to stroke or MI. Patients with pre-existing mental disorders, patients on beta blockers or oral anticoagulants such as warfarin, anti-depressants including sertraline and refusing to provide written informed consent were excluded.

Study procedure

After obtaining consent form, demographic information and clinical data were gathered using a data collection performa. Lipid profiles, Apolipoprotein A and B (Apo A), (Apo B), Coagulation parameters, including Prothrombin Time (PT), and International Normalized Ratio (INR), Partial Thromboplastin Time (PTT) levels were recorded both at baseline and after 24 weeks of sertraline therapy. The study participants were categorized as 2 groups: Patients diagnosed with depression who had experienced a MI were in group A, while Group B included patients diagnosed with depression following a stroke. For those newly diagnosed with depression, sertraline tablets were prescribed at a dosage of 50 mg, to be taken twice daily alongside their standard medications. The treatment response was evaluated using the HAM-D scale. This was assessed both before and after the initiation of sertraline therapy over a period of 24 weeks. Additionally, medication adherence and Quality of Life (QoL) were measured at baseline and at week 24 by employing the Medication Adherence Rating Scale (MARS) and RAND-36 questionnaires.

Statistical analysis

Data analysis was conducted on Windows, utilizing SPSS version 29.0. Descriptive statistics were used to characterize the data, with n (%) used for categorical variables and the mean (SD) and median (IQR) for continuous variables. To check the normality of the data, the Shapiro-Wilk test was conducted. For between-group comparisons, the Mann-Whitney U test was employed, and Friedman's test was applied, with subsequent pairwise comparisons using the Wilcoxon Signed Ranks test and Bonferroni correction was used for within-group comparisons. The Chi-square test was applied to assess the significance of categorical data. All statistical tests were two-tailed, with a $p<0.05$ was considered the threshold for significance in all the aforementioned statistical tools and all of the statistical tests performed were two-sided.

RESULTS

The study screened 148 patients totally and separated the participants into two distinct groups: group A included patients with depression due to MI, and group B included patients with depression following a stroke. Both groups received a prescription for a tablet containing 50 mg sertraline. There were a total of 19 dropouts, with 12 in group A and 7 in group B. Finally, 129 out of 148 patients met the eligibility criteria for inclusion, with 62 individuals assigned to group A and 67 to group B. Their demographic details are presented in Table 1. The occurrence of depression among MI and stroke patients was observed more frequently in males than in females. The median age for participants in group A was 52.24±2.7 years, whereas in group B, it was 53.4±3.2 years, showing no significance between the groups ($p=0.474$).

After using sertraline for 24 weeks, group B exhibited improved control over total cholesterol levels (from 161.1±17.5 mg/dL to 149.3±14.9 mg/dL), LDL (from 111.5±17.5 mg/dL to 110.4±16.4 mg/dL), and HDL (from 52.6±10.4 to 55.2±11.1) in comparison to group A. Blood pressure readings, HbA1c levels, showed stability in both the groups and no significant ($p>0.05$) alterations were noted in coagulation parameters. Table 2 shows post-stroke patients showed a more favourable response in TC, HDL, LDL and TG levels compared to post MI patients, but this difference was not statistically significant.

Between group, revealed a significant improvement of HAM-D at week 24 ($p=0.029$). In the within-group comparison, improvement was observed from week 16 onwards, with group B demonstrating better clinical improvement in HAM-D scores compared to group A, indicating a stronger response in post-stroke patients, as depicted in Table 3.

The medication adherence scores from the MARS Questionnaire for both groups during the treatment period was depicted in Table 4. Both groups exhibited no statistically significant differences at the end of the treatment period (week 24). On assessing health-related quality of life through RAND-36 scores, both groups showed improvement in overall well-being. Statistically significant improvements were observed (p=0.043) only in the physical well-being and role limitation due to emotional health (p=0.022) at the week 24.

Table 1: Baseline demographics of study patients.

Characteristics	Group A *N*=62 (%)	Group B *N*=67(%)	*p*-value
Age	52.24±2.7	53.4±3.2	0.474#
Gender			
Male	35 (56.4)	42 (62.6)	0.470#
Female	27 (43.5)	25 (37.3)	
Occupation			
Employed	23 (37)	24 (35.8)	0.977#
Unemployed	34 (54.8)	37 (55.2)	
Business	05 (8)	06 (10.4)	
Education			
Middle/high school	36 (58)	43 (64.1)	0.579#
Undergraduate	21 (33.8)	17 (25.3)	
Postgraduate	05 (8)	07 (10.4)	
Disease duration (years)	2.5±1.6	2.2±1.8	0.101#
Marital status			
Single	15 (24.1)	21 (31.3)	0.368#
Married	31 (50)	24 (35.8)	
Separated	09 (14.5)	08 (11.9)	
Divorced	03 (4.8)	08 (11.9)	
Widowed	04 (6.4)	06 (8.9)	
Family type			
Nuclear	30 (48.3)	33 (49.2)	0.435#
Joint	21 (33.8)	24 (35.8)	
Extended	07 (11.2)	09 (13.4)	
Living alone	04 (6.4)	01 (1.4)	
Socioeconomic class			
Upper	05 (8.0)	04 (5.9)	0.172#
Upper middle	12 (19.3)	09 (13.4)	
Lower middle	24 (38.7)	16 (23.8)	
Upper lower	14 (22.5)	25 (37.3)	
Lower	07 (11.2)	13 (19.4)	
Co-morbidities			
DM	15 (24.1)	18 (26.8)	0.603#
HTN	18 (29.0)	17 (25.3)	
Hyperlipidaemia	9 (14.5)	10 (14.9)	
DM + HTN	10 (16.1)	9 (13.4)	
Hyperthyroidism	5 (8.0)	4 (5.9)	
No comorbidities	5 (8.0)	9 (13.4)	

*** <0.001; Very highly significant; ** <0.01; Highly significant; *< 0.05; Significant; # >0.05; No significant.

DISCUSSION

This study divided patients into two groups: A, who had depression after a MI, and B, who had it after a stroke. Demographics showed normalized age, gender, education, employment, marital status, and family type across both groups. The individuals with cardiovascular and cerebrovascular diseases is rising rapidly, exposing middle-aged and older patients at risk (Yan & Hu, 2024). The patients in both the MI and stroke groups suffering from depression were between the ages of 51 and 60 years, concordant with our studies. In this study, we prescribed sertraline as the antidepressant of choice, focusing on its efficacy in treating depression among patients with MI and stroke.

Both groups had consistent HAM-D score reductions during treatment. This study found that sertraline significantly reduced depressive symptoms in stroke patients more than in MI patients, suggesting a better response to sertraline in stroke patients. This is possibly due to the complex relationship between depression and stroke-related neurological changes. Better clinical progress was seen in group B, which had higher response, remission, and relapse rates than group A. Differences were not statistically significant. In studies of coronary artery disease, including MI, sertraline reduced HAM-D scores and improved clinical outcomes (Blumenthal *et al.*, 2012). Research by Bour *et al.*, indicated that individuals suffering from depression after a stroke tend to exhibit unique symptoms compared to those with post-MI depression. Stroke patients more frequently show signs of loss of interest, psychomotor slowing, and vegetative symptoms, which are directly linked to the neurological impact of the stroke. In contrast, MI-related depression often arises from the sudden and life-threatening nature of the heart condition (Bour *et al.*, 2009). Our findings suggest that the neurological factors involved in stroke may make these patients more responsive to sertraline treatment for depression, mirroring Bour *et al.*, findings of the distinct nature of depression in stroke versus MI participants.

A meta-analysis found that many MI and stroke patients go untreated for depression, highlighting the need for better intervention strategies (Ladwig *et al.*, 2018). Sertraline worked for both groups, but stroke patients responded better. This suggests cardiovascular patients need structured depression treatment. This study confirms the literature review that sertraline reduces depressive symptoms, especially in MI and stroke survivors. Sertraline's safety, especially its low QT interval effect compared to other SSRIs, supports its use in this population (Zambrano *et al.*, 2020). Contrary to our findings, a trial concluded that treatment with sertraline did not result in better improvements

Table 2: Clinical parameter response to sertraline treatment between the groups.

Clinical Parameters	Treatment period	Group A (*N*=62)	Group B (*N*=67)	*p*-value
TC	Week 0	158.5±17.2	161.1±17.5	0.981#
	Week 24	153.2±15.6	149.3±14.9	
LDL	Week 0	111.2±20.7	111.5±17.5	0.366#
	Week 24	115.1±18.2	110.4±16.4	
TG	Week 0	142.4±14.1	144.5±13.2	0.261#
	Week 24	134.2±13.6	132.4±10.2	
Apo A	Week 0	26.9±3.8	27.4±4.6	0.649#
	Week 24	26.1±3.7	27.6±4.2	
Apo B	Week 0	105.3±12.3	106.7±11.8	0.827#
	Week 24	105.1±17.2	106±11.6	
SBP	Week 0	128.8±10.5	127.8±10.6	0.575#
	Week 24	127.9±10.9	126.7±9.9	
DBP	Week 0	78.7±4.1	79.4±3.9	0.490#
	Week 24	78.2±3.1	78.9±3.5	
PTT	Week 0	28.9±1.9	29.0±1.6	0.790#
	Week 24	29.5±1.8	29.9±2.0	
PT	Week 0	10.5±0.7	10.7±1.0	0.861#
	Week 24	10.8±1.2	11.1±1.2	
INR	Week 0	0.9±0.12	0.9±0.17	0.474#
	Week 24	0.8±0.23	0.9±0.1	

*** <0.001; Very highly significant; ** <0.01; highly significant; *< 0.05; Significant; # >0.05; No significant.

in symptoms of depression or cardiovascular conditions. Several other studies have also demonstrated enhanced depression outcomes in stroke patients treated with sertraline (Rasmussen *et al.*, 2003; Stuckart *et al.*, 2021).

Lipid profiles, blood pressure, HbA1c, and coagulation markers were examined in both groups to determine sertraline response. Group B's lipid profiles improved, while Group A's rose significantly from baseline. In both groups, the remaining clinical parameters changed minimal, reflecting only minor responses. A study of sertraline and fluoxetine in depression and diabetes patients found that sertraline reduced lipid profiles (Bayani *et al.*, 2024). But it raised triglycerides compared to before treatment (Kesim *et al.*, 2011). Multiple studies have shown that sertraline worsens lipid profiles, which may increase lipid levels in certain patients (Wei *et al.*, 2009; Beyazyüz *et al.*, 2013). To avoid cardiovascular side effects, we should monitor patient's lipid levels during sertraline treatment. Another study confirmed our findings that blood pressure and HbA1c levels were stable during treatment (Padmapriya *et al.*, 2020; Kesim *et al.*, 2011). Sertraline may improve glycemic control, but its effects on BP are unclear (Bayani *et al.*, 2024). According to research, people who take sertraline have coagulation scores that are similar to those of healthy people. A few reports of bleeding issues have surfaced, but they don't appear to be associated with changes in coagulation metrics. Therefore, it appears that sertraline has a minimal impact on coagulation (Geiser *et al.*, 2011). Prior studies suggested that sertraline in depression patients with any coronary events could increase platelet inhibition in addition to concomitant medications (Serebruany *et al.*, 2003).

On comparing medication adherence, both groups demonstrated improved medication adherence. However, at the terminal phase of treatment, group B showed a numerical improvement in their MARS score compared to group A. Prior research has indicated that poor adherence to medication can worsen depression in cardiovascular conditions, highlighting the importance of consistent treatment (Ladwig *et al.*, 2018). In contrast, a meta-analysis suggests that both post-MI and post-stroke conditions negatively impact medication adherence, increasing the risk of adverse health outcomes. The present study explains the greater reduction in depression symptoms in both groups, especially in group B, which suggests that improving adherence could be a key factor in enhancing treatment outcomes for depression in patients with cardiovascular conditions.

Assessing HRQoL helps understand the broader impact of treatments, guiding interventions that aim to improve daily functioning and long-term health outcomes for individuals with cardiovascular diseases. In this study, by the 24th week, both groups experienced improvements in HRQoL (Rahman *et al.*,

Table 3: Between and within group comparison of sertraline from baseline to week 24.

Treatment period (Week)	HAM-D score		
	Group A (*n*=62)	Group B (*n*=67)	*p*-value
0	16.92±1.1	17.01±1.3	0.428$^{\#}$
4	16.84±1.5	16.75±1.1	0.322$^{\#}$
8	15.58±1.4	16.10±1.3	0.119$^{\#}$
12	14.67±1.7	14.69±1.1	0.327$^{\#}$
16	11.69±1.0**	10.70±1.1**	0.139$^{\#}$
20	8.50±1.1**	8.59±1.2**	0.217$^{\#}$
24	5.98±1.2***	3.54±1.1***	0.029*

*** <0.001; Very highly significant; ** <0.01; highly significant; *< 0.05; Significant; # >0.05; No significant.

Table 4: Between and within groups comparison of medication adherence using MARS Questionnaire.

Treatment period (Week)	MARS Score		*p*-value
	Group A (*N*=62)	Group B (*N*=67)	
4	5.4±1.3	6.0±1.1	0.231$^{\#}$
8	6.4±1.0	6.9±0.8	0.346$^{\#}$
12	7.0±1.0	7.7±1.5	0.216$^{\#}$
16	7.5±1.4	7.9±0.9	0.244$^{\#}$
20	7.9±1.5**	8.2±1.3**	0.334$^{\#}$
24	8.4±1.2**	8.9±0.7**	0.146$^{\#}$

*** <0.001; Very highly significant; ** <0.01; highly significant; *< 0.05; Significant; # >0.05; No significant.

2024). However, group B demonstrated clinically better outcomes in all eight specific domains than group A. Research suggests that sertraline not only lowers depression levels but also positively impacts HRQoL over time (Lavu *et al.*, 2022)

CONCLUSION

This study examines how sertraline affects depressive symptoms in MI and stroke patients, highlighting the link between cardiovascular health and mental health. Results showed significant improvements in depression, with post-stroke patients responding better to treatment than post-MI patients, as reflected in HAM-D scores. Improvements in clinical parameters, medication adherence, and quality of life were notable, especially in the stroke group. The findings emphasize the need for holistic strategies to manage both mental and physical health in cardiac patients with depression.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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