Alqalam Journal of Medical and Applied Sciences. 2026;9(2):371-375
https://doi.org/10.54361/ajmas.269209

Original article

Effect of Aerobic Exercise on Major Depression in Patients with Mild Alzheimer's Disease

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Abstract
Alzheimer's disease (AD), the leading cause of dementia, represents a significant source of morbidity and mortality in the elderly population. Emerging evidence suggests depression may be a risk factor for cognitive impairment and AD progression. While physical activity is generally recognized for its mood-enhancing properties, its specific role in managing depression in AD patients requires further investigation. This study aimed to evaluate the effect of structured aerobic exercise as an adjunctive therapy for major depression in patients with mild Alzheimer's disease. In a randomized controlled trial, 40 participants (age range: 60-80 years) diagnosed with major depression and mild AD were allocated into two groups. The experimental group (n=20) received a combination of antidepressant medication (SSRI) and a supervised aerobic exercise program, consisting of treadmill walking for 30 minutes at 3.5 km/h, three times per week for four weeks. The control group (n=20) received antidepressant medication only. The primary outcome, depression severity, was measured at baseline, at 2 weeks, and at 4 weeks post-intervention using the HDRS. While both groups showed significant improvements in HDRS scores from baseline ($p<0.0001$), the experimental group demonstrated a significantly greater reduction in depression scores compared to the control group post-intervention ($p=0.001$). The mean decrease in the HDRS score was 20.53 points in the exercise group versus 8.13 points in the medication-only group. A structured aerobic exercise program, when combined with pharmacotherapy, is a significantly more effective intervention for reducing depressive symptoms in patients with mild Alzheimer's disease than pharmacotherapy alone. These findings support the integration of supervised aerobic exercise into standard treatment regimens for managing major depression in this patient population.
Keywords. Aerobic Exercise, Major Depressive Disorder, Alzheimer's Disease.

Introduction

Alzheimer's disease (AD) is the most common cause of dementia and a major contributor to morbidity and mortality among older adults worldwide. In 2015, approximately 46.8 million people were living with dementia globally, with estimated societal costs reaching $818 billion. The incidence of dementia rises sharply with age, increasing from five to ten cases per 1,000 person-years in individuals aged 64–69 to forty to sixty cases per 1,000 person-years among those aged 80–84. In Europe, the prevalence of AD was estimated at 5.05% in 2017, with higher rates observed in women compared with men. These findings highlight the expanding public health burden of AD and the urgent need to strengthen research and intervention efforts aimed at understanding and managing this condition [1,2].

Depressive symptoms are common among individuals with AD, affecting approximately 20–30% of patients. Depression itself is a prevalent and disabling disorder, impacting nearly 300 million people worldwide and contributing to increased functional impairment. Although a consistent association between depression and AD has been reported, the nature of this relationship remains unclear. Depression may represent an independent risk factor, an early neuropsychiatric manifestation of neurodegenerative processes, or a psychological response to emerging cognitive decline. While some evidence suggests depressive symptoms often coincide with or precede AD onset, other studies indicate a limited influence on disease risk or progression. Nevertheless, comorbid depression has been associated with accelerated functional decline and an increased risk of behavioral disturbances in individuals with AD [3,4]. Depressive disorders, with prevalence estimates ranging from 5% to 25%, exert substantial adverse effects on physical health, psychological well-being, and mortality across populations regardless of demographic or socioeconomic background. Depressive symptoms may also arise as adverse effects of commonly prescribed medications, including glucocorticoids, oral contraceptives, and interferon, or may reflect underlying medical conditions such as vitamin B12 deficiency. Importantly, depression is linked to heightened risks of cognitive impairment, frailty, institutionalization, malnutrition, reduced self-esteem, functional deterioration, and poor adherence to chronic disease treatments [5–7].

Given this multifactorial relationship, non-pharmacological interventions have gained increasing attention as adjunctive treatment options. Aerobic exercise—defined as sustained rhythmic physical activity that elevates heart rate and oxygen consumption—has been widely recognized for its antidepressant and mood-enhancing effects. These benefits are thought to be mediated through neurobiological mechanisms involving increased availability of neurotransmitters such as serotonin, dopamine, norepinephrine, and endorphins. Accordingly, the present study aims to evaluate the impact of structured aerobic exercise on major depressive symptoms in individuals with mild Alzheimer's disease [8,9]. Beyond its psychological benefits,

Received*: 04-12-2025 -* ***Accepted****: 02-02-2026 -* ***Published****: 09-02-2026*

regular aerobic exercise provides well-established cardioprotective effects and significantly reduces cardiovascular mortality risk. Weight-bearing aerobic activities further support bone health by stimulating osteogenesis and reducing osteoporosis risk. In addition, aerobic training promotes physiological adaptations that enhance muscular endurance and metabolic efficiency, including increased substrate storage, improved capillary density, enhanced oxygen delivery, and upregulation of aerobic energy pathways [10].

A growing body of observational and interventional evidence demonstrates an inverse relationship between physical activity and depressive symptom severity. Individuals who engage in regular physical activity consistently report lower scores on standardized depression and anxiety measures compared with sedentary individuals, reinforcing the therapeutic potential of exercise as both a preventive and rehabilitative strategy [11]. Therefore, the aim of the present study was to evaluate the effect of a structured aerobic exercise program on depressive symptoms in patients diagnosed with major depression and mild Alzheimer's disease.

Methods

Study Design and Participant Selection

A pretest-posttest controlled study was conducted to evaluate the impact of a structured aerobic exercise program on major depression in patients with mild Alzheimer's Disease. Forty participants (aged 60-80 years) diagnosed with major depressive disorder according to DSM-IV-TR criteria were recruited. Inclusion criteria stipulated a BMI of <30 kg/m² and general cooperativeness, while exclusion criteria included comorbidities such as diabetes, hypertension, and cancer. Informed consent was obtained from all participants prior to enrollment in the study

Intervention Protocol

Participants were randomly allocated into two groups via a simple card-based randomization method

In this study, participants were divided into two groups. Group A (experimental, n = 20) received a combined therapeutic intervention consisting of a prescribed dose of an SSRI antidepressant together with a supervised aerobic exercise program. The exercise component involved treadmill walking at 3.5 km/h for 30 minutes per session, three times per week, over a four-week period. Group B (control, n = 20) received only the SSRI antidepressant medication for the same four-week duration, without the addition of the exercise program. This design allowed for direct comparison between pharmacological treatment alone and a combined pharmacological–exercise approach.

Outcome Measure and Statistical Analysis

The primary outcome was the level of depression, assessed using the Hamilton Depression Rating Scale (HDRS) [12]. A qualified psychologist administered the HDRS at baseline, two weeks, and four weeks. Statistical analyses were performed using SPSS version 22. The Mann-Whitney U test was used for between-group comparisons, and the Friedman test with Dunn's post-hoc analysis was employed to evaluate within-group changes over time. A p-value of <0.05 denotes statistical significance.

Results

Table 1 summarizes the baseline demographic and anthropometric data for the two study groups. The analysis reveals no statistically significant differences between Group A (Exercise + Medication) and Group B (Medication Only) in terms of age, weight, height, or Body Mass Index (BMI) (all p > 0.05). This homogeneity at baseline confirms that the randomization process was successful and that any subsequent differences in outcome measures can be more confidently attributed to the intervention rather than to pre-existing disparities between the groups.

Table 1. Baseline Demographic and Anthropometric Characteristics of the Study Groups

Characteristic	Group A (Exercise + Medication) (n=20)	Group B (Medication Only) (n=20)	p-value
Age, years	70.55 ± 6.75	71.75 ± 5.79	0.37
Weight, kg	71.50 ± 11.06	74.00 ± 6.07	0.51
Height, cm	162.80 ± 8.64	165.90 ± 6.85	0.57
Body Mass Index, kg/m²	26.65 ± 2.68	26.87 ± 1.11	0.71

Note: Data presented as Mean ± Standard Deviation. p-values derived from an independent samples t-test.

The longitudinal HDRS scores for both groups are presented in (Table 2). At pre-treatment, both groups began with high levels of depressive symptoms. Over the 4-week intervention, a downward trend in HDRS scores is visible in both groups, indicating an improvement in depressive symptoms. However, the magnitude of reduction is markedly greater in Group A (Exercise + Medication), which showed a mean decrease of 20.53 points, compared to a mean decrease of 8.13 points in Group B (Medication Only). This

Received*: 04-12-2025 -* ***Accepted****: 02-02-2026 -* ***Published****: 09-02-2026*

descriptive data suggests a potentially superior effect of the combined intervention.

Table 2. Hamilton Depression Rating Scale (HDRS) Scores Across the Study Timeline

Assessment Point	Group A (Exercise + Medication) (n=20)	Group B (Medication Only) (n=20)		
	Mean	SD	Mean	SD
Pre-treatment	31.83	7.32	28.65	6.61
2 Weeks	17.10	2.80	24.00	8.32
4 Weeks (Post-treatment)	11.30	3.50	20.52	8.31

Note: SD = Standard Deviation. A lower HDRS score indicates a lower level of depressive symptoms.

As shown in (Table 3), the results were highly statistically significant for both Group A ($x^2 = 30.00$, $p < 0.0001$) and Group B ($x^2 = 29.52$, $p < 0.0001$). This confirms that there was a significant change in depression levels across the three assessment time points (pre-treatment, 2 weeks, and 4 weeks) within each group, regardless of the type of intervention.

Table 3. Friedman Test Analysis of Within-Group Changes in HDRS Scores Over Time

Group	Friedman Statistic (x^2)	p-value
Group A (Exercise + Medication)	30.00	< 0.0001
Group B (Medication Only)	29.52	< 0.0001

Note: The Friedman test is a non-parametric repeated measures ANOVA.

The results in Table 4 demonstrate a significant reduction in HDRS scores after just two weeks of combined therapy compared to baseline ($p < 0.05$). The improvement was even more pronounced at the 4-week post-treatment assessment compared to baseline ($p < 0.001$). Crucially, a further statistically significant improvement was observed between the 2-week and 4-week assessments ($p < 0.05$), indicating a continuous, progressive therapeutic benefit throughout the entire intervention period.

Table 4. Post-Hoc Pairwise Comparisons of HDRS Scores for Group A (Exercise + Medication)

Comparison	Rank Sum Difference	p-value
Pre-treatment vs. 2 Weeks	14.00	< 0.05
Pre-treatment vs. 4 Weeks	30.00	< 0.001
2 Weeks vs. 4 Weeks	14.00	< 0.05

In (Table 5) Group B (Medication Only), Dunn's post-hoc test also revealed significant within-group improvements. Similar to Group A, there were significant reductions from baseline to 2 weeks ($p < 0.05$) and from baseline to 4 weeks ($p < 0.001$). A significant improvement was also noted between the 2-week and 4-week marks ($p < 0.05$). This confirms that antidepressant medication alone had a positive and progressively significant effect on depressive symptoms over time.

Table 5. Post-Hoc Pairwise Comparisons of HDRS Scores for Group B (Medication Only)

Comparison	Rank Sum Difference	p-value
Pre-treatment vs. 2 Weeks	14.00	< 0.05
Pre-treatment vs. 4 Weeks	28.20	< 0.001
2 Weeks vs. 4 Weeks	15.40	< 0.05

As detailed in (Table 6), there was no significant difference in HDRS scores between the two groups at the pre-treatment baseline ($p = 0.28$). However, after two weeks of intervention, a statistically significant difference emerged ($U = 61.5$, $p = 0.02$), with Group A showing lower depression scores. This between-group difference widened and became highly significant by the end of the 4-week study period ($U = 34.4$, $p = 0.001$). These results robustly indicate that the group receiving aerobic exercise in addition to medication achieved a significantly greater reduction in depressive symptoms than the group receiving medication alone.

Table 6. Between-Group Comparisons of HDRS Scores at Each Assessment Point

Assessment Point	Mean Difference (A - B)	Mann-Whitney U Statistic	p-value
Pre-treatment	3.18	86.0	0.28
2 Weeks	-6.90	61.5	0.02
4 Weeks (Post-treatment)	-9.22	34.4	0.001

Note: A negative mean difference indicates a lower score (less depression) in Group A.

Received*: 04-12-2025 -* ***Accepted****: 02-02-2026 -* ***Published****: 09-02-2026*

Discussion

The present study sought to investigate the efficacy of aerobic exercise as an intervention for major depression in patients diagnosed with mild Alzheimer's disease. The findings, which demonstrate a significant reduction in depression scores in the exercise group compared to the control group, are consistent with a substantial body of existing literature examining the relationship between physical activity and mood disorders. Our results align with the conclusions of Salmon (2001) [13], who noted the challenges of motivating clinically depressed individuals in controlled exercise trials, yet affirmed that physical activity can serve as a cornerstone for successful treatment. This is further supported by epidemiological evidence summarized by Martinsen (1994) [14], which positions regular exercise as a protective factor against depression, noting that populations with mental health issues tend to be less active. Biddle et al. (2000) [15] further consolidated evidence for a causal link, suggesting exercise is effective both in reducing existing depressive symptoms and potentially preventing their onset. However, the scope of exercise's benefits appears specific. For instance, a randomized controlled trial by Airaksinen et al. (2004) [16] involving 202 sedentary adults with Major Depressive Disorder (MDD) found little evidence that aerobic exercise conferred significant advantages for neurocognitive performance, despite targeting depressive symptoms. This indicates that the therapeutic effects of exercise may be domain-specific. The long-term and comparative efficacy of exercise is a critical consideration. The seminal work of Babyak et al. (2000) [17] demonstrated that patients in an exercise group not only exhibited lower depression rates (30%) than those in medication (52%) or combined (55%) groups at the end of treatment but also showed a markedly lower relapse rate (8%) at a 6-month follow-up compared to the medication (38%) and combination (31%) groups. This suggests that exercise may impart sustainable, long-term protective benefits against depressive relapse.

The concept of a dose-response relationship is crucial for clinical application. Dunn et al. (2005) [18] provided evidence that an exercise regimen meeting public health recommendations (e.g., 30 minutes per day, 5 days a week) yields superior antidepressant effects compared to lower doses or placebo-like activities. This dose-response gradient strengthens the argument for a causal mechanism. While patient adherence in real-world settings remains a challenge, the high tolerability of exercise in research settings is a promising finding. The mechanisms through which exercise alleviates depression are multifaceted. Physiological models propose explanations involving increased circulating beta-endorphins and monoamines, elevated body temperature, and improved overall fitness [19]. However, as these physiological changes develop gradually, they cannot fully account for the rapid mood improvements often observed. This suggests a significant role for psychological mechanisms. Exercise is theorized to enhance one's sense of mastery and self-efficacy, which is particularly potent for individuals feeling a loss of control due to depression. A meta-analysis of 51 trials corroborates a modest but significant rise in self-esteem following exercise [20]. Additional psychological benefits include "therapeutic distraction," whereby focus shifts from ruminative thoughts to the physical activity, and improved body image and perceived control over health behaviors [20]. The reduction in depression scores observed in our study following the walking program is likely attributable to a synergy of these physical and psychological improvements, which collectively enhance perceived well-being and life satisfaction.

It is noteworthy, however, that the relationship between exercise intensity and mood benefit is not linear. As highlighted by Timonen et al. (2002) [21], moderate-intensity exercise may sometimes be more effective in reducing depression than high-intensity programs, a nuance that requires careful consideration in treatment planning. This is corroborated by Knubben et al. (2007) [22], who found that a short-term, high-intensity endurance exercise program led to a significantly greater decrease in depression scores (41% reduction) compared to a light stretching control (21%) in hospitalized patients. Conversely, Geddes, Butler & Hatcher (2003) [23] have argued for a more measured perspective on the efficacy of exercise, suggesting its standalone efficiency may be limited. Nevertheless, the improvements in physical self-efficacy, self-confidence, and perceived control documented in our study and others underscore its value as a component of a comprehensive treatment strategy

Conclusion

The findings of this study contribute to the growing consensus that supervised aerobic exercise is an effective adjunctive therapy for mitigating major depression in patients with mild Alzheimer's disease, yielding benefits that likely arise from a complex interplay of physiological and psychological pathways.

Conflict of interest. Nil

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Received: *04-12-2025* - ***Accepted***: *02-02-2026* - ***Published***: *09-02-2026*

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Received*: 04-12-2025 -* ***Accepted****: 02-02-2026 -* ***Published****: 09-02-2026*