

Is Physical Inactivity A Risk Factor Of Dementia? A Case Control Study among Clinically Diagnosed Dementia Patients in Chennai**Shaamir Faraz¹, Kamali R.², Sathish Kumar K.³, S. Arunmurugan⁴, Kamali R.⁵**¹Junior Resident, Department of Family Medicine AIIMS, Jodhpur, Rajasthan, India²Associate Professor, Department of Community Medicine, Government Medical College, Dindigul, Tamil Nadu, India³Associate Professor, Department of Community Medicine, Government Medical College, Omandurar Government Estate, Chennai, Tamil Nadu, India⁴Professor & HOD, Department of Community Medicine Government Medical College, Omandurar Government Estate, Chennai, Tamil Nadu, India

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Abstract**Background:** Regular exercise has been shown to have a neuroprotective impact on cognitive function over the long term, lowering the risk of dementia and delaying its onset. We conducted a study to determine the correlation between physical inactivity during midlife and occurrence of dementia in later life.**Materials and Methods:** A Sample of 47 clinically diagnosed dementia patients according to ICD -11 /DSM -5 and 47 age, sex and locality matched controls were chosen for the study. Basic socio-demographic details and Questions regarding the physical activity they did during their midlife in different domains like work, travel and recreational activities were collected. A validated questionnaire- GPAQ questionnaire was used to collect data about physical activity. The data collected was entered in excel and analyzed with IBM SPSS software version 21.**Results:** The mean age of the participants was 67.57 ± 7.27 with the minimum age being 54 and the maximum age being 85. About 46.8% of the respondents were males. The amount of physical activity by controls was significantly higher as compared to the cases as measured categorized by work, recreational, travel and total METs. Those who were doing low physical activity and are in the high risk group have more risk of getting dementia [OR = 24.5 (7.87-76.27)]. The risk increases after adjusting for age, gender, education, occupation, presence of diabetes and presence of hypertension. [aOR = 31.5 (13.2 – 54.1)].**Conclusion:** Physical inactivity during midlife is a significant predictor for the onset of dementia in later life.**Keywords:** Dementia, Physical activity in midlife, GPAQ, Metabolic Equivalents (METs), Case – control study.**DOI:** 10.25258/ijcpr.18.8.56

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Introduction

Dementia refers to a decline in cognitive performance that is more than what would be predicted given the typical effects of biological aging. [1]. Cognitive decline is a recognized warning sign of Alzheimer's disease or moderate cognitive impairment. Most of the time, people with cognitive decline do experience memory loss, including forgetfulness and an inability to perform as routinely or objectively as they formerly did. [2,3] The illness may be stable or progressing, irreversible or curable.

The underlying clinical state and the availability and administration of appropriate treatment are related to the potential reversibility of dementia. If treatment is started before permanent damage

occurs, 15% of dementia patients have treatable conditions. [4] Dementia can be associated with numerous disorders of the central nervous system or any traumatic injury to the brain. In 2015, approximately 5% of the global elderly population, which amounts to 47 million individuals, experienced dementia. This number is expected to rise to 75 million by 2030 and 132 million by 2050. Recent assessments indicate that there are approximately 9.9 million instances of dementia occurring globally on an annual basis, which equates to a new case emerging every three seconds and about 55 million prevalent cases of dementia are existing in the world.

At present, approximately 60% of dementia cases are found in low- and middle-income countries, and it is projected that these same nations will be responsible for 71% of new cases. [5,6] Currently, there are more than 55 million individuals globally who are already afflicted with dementia, and an additional 10 million new cases are documented every year. [1] There are several causes of dementia, such as traumatic brain injury, HIV, Parkinson's disease, Alzheimer's disease, dementia with Lewy bodies, vascular dementia, frontotemporal dementia, and Huntington's disease. [4] Alzheimer's disease accounts for 60–70% of dementia cases, making it the most common kind of the illness. Physical inactivity, cardiovascular disorders, and associated risk factors such as middle-aged obesity, smoking, hypertension, and diabetes are modifiable risk factors for dementia. [7] Depression has been found to be one of the modifiable risk factors for Alzheimer's disease, which doubles the chance of acquiring the condition. [8]

More precisely, additional modifiable risk factors linked to dementia include midlife depression, poor educational attainment, social isolation, and cognitive inactivity. Furthermore, an individual's probability of acquiring dementia is increased by innate, unchangeable genetic risk factors. [9]. Dementia is one of the primary causes of impairment and reliance among the elderly globally. The physical, psychological, social, and economical elements of dementia patients' lives are profoundly impacted, as are those of their family members, caregivers, and society at large. [1]. Of all the years spent living with a handicap brought on by a noncommunicable illness, dementia accounts for 11.9%. [10].

The World Health Organization's guidelines include evidence-based strategies to lower the risk of dementia and cognitive decline. These treatments concentrate on treating medical diseases like diabetes and hypertension as well as modifiable risk factors like an unhealthy diet and sedentary lifestyle. 1. Out of all the lifestyle changes that have been studied, regular exercise appears to be one of the greatest ways to reduce your risk of dementia. Several studies examining the effects of aerobic exercise, or heart-pumping physical activity, on middle-aged or older adults have reported improvements in memory retention, cognitive function, and dementia incidence. [11,12] Recent studies show that physical activity reduces the likelihood of elderly Japanese individuals

According to recent research, regular, long-term exercise significantly improves cognition, lowers the risk of dementia, and even slows the progression of dementia. Due to the lack of evidence that medications can protect against dementia, exercise can be a more dependable

option to maintain good brain health by reducing the chance of atherosclerotic cerebrovascular disease. [13]

Research on the advantages of exercise suggests that sustained, regular exercise is necessary to reap these benefits. Although the exact features of the workout cannot be determined, any activity that raises the heart rate and oxygen need can be taken into consideration. These exercises should ideally be done for at least 20 to 30 minutes each session. These aerobic exercises come in many forms, including walking, bicycling, playing basketball, volleyball, football, and even doing housework like sweeping the courtyard. [11-13]

Hence, this study was conducted with the following objectives

Objectives

- To determine the relationship between levels of physical activity done in midlife and occurrence of dementia in later life.
- To compare quantitatively, the physical activity done by the cases and controls during their midlife.

Materials and Methods

This was a case-control study conducted at dementia care centers in Chennai from September 2022 to October 2022. The cases included 47 clinically diagnosed dementia patients according to ICD -11 /DSM -5 aged 50-90 years residing in these centers without complications and controls were 47 Healthy age, sex and locality matched controls. Exclusion criteria were patients with dementia due to traumatic brain injury, those with a family history of dementia, severely ill patients, patients whose caregivers cannot communicate due to language barriers, and patients with alcohol-induced dementia.

The sample size was calculated using Open Source Epidemiologic Statistics for public health sample size calculating software. [14]. From a previous study finding, [12] the proportion of dementia cases with physical activity was 0.6, the proportion of controls with physical activity was 85.71% and the expected odds ratio to be 4% sample size was calculated to be 47 in both groups at 95% confidence level with study power as 95%. Hence data was collected from 47 cases and 47 controls.

The study used convenience sampling, selecting patients attending dementia care centers until the required sample size was reached.

Study Procedure:

The sociodemographic data of the patients were collected from the caretakers. The caretakers of the patients were interviewed regarding the physical activity of the study participants in their midlife

using the Global Physical Activity Questionnaire (GPAQ) [15], which was adapted to fit the requirements of the study.

The Global Physical Activity Questionnaire was developed by the World Health Organization (WHO) to track the amount of physical activity in various nations. Through a series of 16 questions (P1-P16), the survey collects information on sedentary behavior and participation in three domains of physical activity. The following are the three domains

- Work place activity
- Activity done during Travel to and from places
- Recreational activities.

The physical activity done was scored and analysed using Metabolic Equivalents (METs).

METs, short for Metabolic Equivalents, are frequently employed to quantify the level of physical activity and are also utilized in the analysis of GPAQ data. Metabolic equivalent (MET), represents the ratio of an individual's active metabolic rate to their baseline resting metabolic rate. A MET, or metabolic equivalent, is a unit of measurement that represents the energy expenditure of sitting quietly. It is equal to the consumption of 1 kcal/kg/hr. Existing guidelines have been utilized for the analysis of GPAQ data. A person's estimated calorie expenditure increases four times with moderate activity and eight times with strenuous activity compared to sedentary behavior. Thus, when determining an individual's total energy expenditure based on GPAQ data, a value of 4 METs was allocated for the duration of moderate activities, while a value of 8 METs was assigned for the duration of vigorous activities.

In order to evaluate the physical activity, MET scores for each domain and subdomain were computed independently. We considered the kind of physical activity and the number of days per week it is conducted in order to compute a categorical indicator for the total time spent on physical activity throughout a week. The cases and controls were assigned into the following categories based on the study by Lopez et al. [16]

High Risk: People who have done physical activity accounting to less than 600 MET minutes per week

Moderate Risk: People who have done physical activity accounting for 600-3000 MET minutes per week

Low Risk: People who have done physical activity accounting to more than 3000 MET minutes per week.

Ethical Issues: Ethical considerations were paramount throughout the study. Institutional Ethics Committee approval was sought prior to the conduct of the study. Participants were fully informed about the study's purpose and provided with an information sheet and consent form. For participants with dementia unable to give consent, family consent was obtained.

Participants were also educated about their right to withdraw at any time. Data confidentiality was ensured, with participants identified by code numbers, and data stored securely and used only for research purposes. Privacy was assured during interviews and in the final report, with all identifying information protected. Participation was voluntary, and participants were not obligated to take part. The study maintained accuracy in reporting and proper attribution of ideas and contributions.

Data analysis: The collected data was examined for consistency and completeness. IBM SPSS version 21 software was used for data entry and analysis. We used descriptive statistics such as means and percentages. We unpaired t test in case of quantitative data and the Chi square test in case of categorical data for inferential analysis. Multiple logistic regression was used for multivariate analysis while binary logistic regression was used for bivariate analysis. A statistically significant P value was defined as one that was less than 0.05.

Results

47 Cases and 47 Controls were asked about their physical activity done during midlife, (in case of patients, to their caregivers) and accordingly the GPAQ Questionnaire was filled. The following data was obtained.

All 94 participants among cases and controls were almost equally distributed in age, gender, socio-economic status, education and occupation as shown in Table 1.

The mean age of the study population was 67.57 ± 7.27 with the minimum age being 54 and the maximum age being 85. About 46.8% of the respondents were males. Out of 47 cases, 11 cases were found to be Hypertensive, 14 cases were found to be diabetic. Out of 47 controls, 2 controls were found to be hypertensive and 21 controls were found to be diabetic.

Table 1: Sociodemographic Characteristics of the Participants

Variables	Parameters	Total*	Cases	Controls
Age In Years	50 To 60	20 (21.3)	10 (50.0)	10 (50.0)
	61 TO 70	40 (42.6)	20 (50.0)	20 (50.0)
	71 TO 80	30 (31.9)	15 (50.0)	15 (50.0)
	81 TO 90	4 (4.3)	2 (50.0)	2 (50.0)
Gender	Male	44 (46.8)	22 (50.0)	22 (50.0)
	Female	50 (53.2)	25 (50.0)	25 (50.0)
Education	Below Primary	2 (2.1)	1 (50.0)	1 (50.0)
	Primary	19 (20.2)	8 (42.1)	11 (57.9)
	Secondary	19 (20.2)	10 (52.6)	9 (47.4)
	Higher Secondary	23 (24.5)	13 (56.5)	10 (43.5)
	Graduate	19 (20.2)	9 (47.4)	10 (52.6)
	Post Graduate	12 (12.8)	6 (50.0)	6 (50.0)
Occupation	Professional	13 (13.8)	6 (46.2)	7 (53.8)
	Semi Professional	15 (16.0)	8 (53.3)	7 (46.7)
	Skilled	18 (19.1)	10 (55.6)	8 (44.4)
	Semi-Skilled	8 (8.5)	3 (3.8)	5 (96.2)
	Unskilled	12 (12.8)	7 (5.8)	5 (94.2)
	Unemployed	28 (29.8)	12 (42.9)	16 (57.1)
Diabetes	Yes	35 (37.2)	14 (40.0)	21 (60.0)
	No	59 (62.8)	33 (55.9)	26 (44.1)
Hypertension	Yes	13 (13.8)	11 (84.6)	2 (15.4)
	No	81 (86.2)	36 (44.4)	45 (55.6)

*Percentages are column wise

Table 2: Mean values of Grand total, Work, Travel and Recreational METs

S. No	Parameters	Cases	Controls	P Value
1	Grand Total METs	507.66 ± 531.21	4095.32 ± 4194.137	<0.001
2	Work METs	76.59 ± 311.05	2617.87 ± 4087.64	<0.001
3	Travel METs	1.19 ± 0.398	1.81 ± 0.449	<0.001
4	Recreational METs	7.66 ± 52.51	204.26 ± 529.56	<0.013

The mean value and standard deviation of Grand total METs in dementia cases (n=47) and controls (n=47) were 507.66 ± 531.21 and 4095.32 ± 4194.137. The mean value and standard deviation of Work METs in dementia cases (n=47) and controls (n=47) were 76.59 ± 311.05 and 2617.87 ± 4087.64. The mean value and standard deviation of Travel METs in dementia cases (n=47) and controls (n=47) were 1.19 ± 0.398 and 1.81 ± 0.449. There was a statistically significant

difference (p<.001) between the two groups. The mean value and standard deviation of Recreational METs in dementia cases (n=47) and controls (n=47) were 7.66 ± 52.51 and 204.26 ± 529.56. (Table 2). The mean values of all the METs categories are higher for the controls compared to the cases [Total METs (P<0.001), Works METS (P<0.001), Travel METs (P<0.001) and Recreational METs (P<0.013)] and they were found to be statistically significant.

Table 3: Association between Physical Activity and Dementia

Physical activity Categories#	Cases	Controls	P value	ODDS ratio with 95% CI	Adjusted ODDS ratio with 95% CI*
High risk	35	5	0.001	24.5 (7.87-76.27)	31.5 (13.2 – 54.1)
Moderate risk	12	23		Ref	Ref
Low risk	0	19			

*Adjusted analysis done by multiple logistic regression after adjusting for age, gender, education, occupation, presence of diabetes and presence of hypertension. #Low risk and moderate risk physical activity categories were merged into a single category in analysis.

Table 3 shows that those who were doing low physical activity and are in the high risk group have more risk of getting dementia [OR = 24.5 (7.87-76.27)]. The risk increases after adjusting for age, gender, education, occupation, presence of diabetes

and presence of hypertension. [OR = 31.5 (13.2 – 54.1)]

Discussion

Remaining physically and mentally healthy is mostly dependent on physical activity. This study has unequivocally demonstrated that dementia patients' physical activity levels were much lower than those of age- and sex-matched controls. The average METs values throughout all domains of observation, including employment, travel, and leisure, yielded identical findings. Based on the amount of physical activity done in MET-minutes per week, it was observed that in the dementia cases, most of them belonged to the high risk category (<600 MET-minutes per week), followed by the moderate risk category (600-3000 MET-minutes per week). Very few or no individuals were seen in the low risk category (>3000 MET-minutes per week). In controls, very less number of controls were seen in the high risk category.

Considering <600 METs minutes per week as a risk factor according to study by Kyu HH et al. [17], the odd's ratio was calculated. It was seen that the odds of dementia cases having low METs is 24.5 times more as compared to odds of controls having low METs.

In a meta-analysis done by Hamer M. and Chida Y. found that persons who engaged in regular, routine exercise, sports, or any other physical activity had a lower chance of getting dementia in later life. [18] Additionally, exercise was shown to induce neurogenesis in the dentate gyrus of the hippocampal region in rats, which is the area responsible for memory and also susceptible to aging in a study done in Australia [19].

In a study done by that used, brain MRI demonstrated that exercise improves blood flow to the dentate gyrus, hence encouraging angiogenesis and neurogenesis there. [20] According to another two studies, frequent moderate-intensity exercise for at least 150 minutes per week enhances cognitive performance and spatial memory. [21,22] Several studies have demonstrated that engaging in regular physical exercise lowers cortisol production and raises serotonin and endorphin release, both of which are beneficial for reducing non-cognitive symptoms of dementia. [22-25]

For those without dementia, regular physical exercise has been demonstrated to provide significant cognitive advantages, as per recent meta-analyses of 29 randomized controlled studies. [26] Significant improvements in executive function, memory, attention, and processing speed were noted, despite the relatively minor difference. These benefits were only shown after 1 to 12 months of exercise, making it impossible to assess the long-term impact of exercise on cerebrovascular illnesses.

Alzheimer's patients experience increasing degeneration of the hippocampal region, which is essential for memory. The area most susceptible to aging is the hippocampus dentate gyrus. [19] Nonetheless, exercise greatly enhances dentate gyrus neurogenesis in animal studies, making this area of the brain one of the few that supports neurogenesis. [20] Brain MRI can quantify the regional hippocampal blood volume, which has been demonstrated to be a neurogenesis biomarker in mice. Applying this to people, three months of aerobic activity led to a substantial increase in the volume of blood in the dentate gyrus of the hippocampal region in a small, prospective, uncontrolled experiment of adults. Dentate gyrus angiogenesis, and hence neurogenesis, were considered to be reflected in this. It was linked to somewhat higher cognitive scores. [21] Exercise classified as aerobic involves raising heart rate and oxygen demand to 60% of maximal. For instance, 150 minutes a week of moderate aerobic activity was found to be adequate to be cognitively protective and linked to both enhanced spatial memory and an increase in hippocampus blood volume in two randomized controlled studies. [27-29] Such moderate-intensity exercises are a realistic goal because most people may not be able to handle strong intensity. Even the American Heart Association recommends comparable levels of physical exercise: vigorous aerobic activity for 20 minutes on three days a week or moderate aerobic activity for at least 30 minutes on five days a week. [27]

Endorphins are feel-good chemicals released by exercise, and studies have shown that regular exercise extends one's happiness for extended periods of time. [23] According to a research published in *The Lancet*, persons who regularly exercised experienced 1.5 fewer days of depression each month compared to non-exercisers. Additionally, it was claimed that the best advantages for mental health came from 45 minutes of exercise three to five times a week. A Harvard Medical School article claims that exercise promotes hippocampal growth, which alleviates depression. Exercise releases endorphins and reduces the synthesis of adrenaline, which can cause anxiety, and cortisol, the stress hormone. [24]

According to studies, increasing physical activity can even help bipolar individuals feel better the day after they work out because it releases serotonin, which lifts their spirits. [28,29] Additionally, it has been discovered that exercise-induced elevation in body temperature impacts the brain's hypothalamic-pituitary-adrenal axis, which enhances mood, and boosts blood circulation in the brain. [16] Studies show that physical activity outside is considerably more healthy than indoors since it can help people feel better emotionally and have more energy. It

can also help people cope with stress, anxiety, and sadness. Exercise not only lifts your spirits but also enhances your brain and central nervous system [17]. Hence according to our study lack of regular physical activity can be attributed as a major risk factor for dementia based on the statistics obtained. So regular physical activity like exercises and sports should be promoted and awareness regarding this should also be raised among the general public. With the current generation moving more and more away from outdoor physical activities and towards virtual modes of recreation and entertainment, the relevance of our study has increased.

Conclusion

Based on other similar studies done in the past and with the results of this study, the role of physical inactivity and the development of dementia can be ascertained. Physical activity have been proved to be neuroprotective and improving cognitive function. According to WHO and American Heart Association, at least 150 minutes of moderate intensity exercise is recommended for adults to live a healthy lifestyle.

This study is unique as it is the first case- control study, to have compared the physical activity of dementia cases and controls and the odd's ratio of 24.5 with a significant p value<.001 was obtained. Since this was a case control study, there is a possibility of recall bias in ascertaining the physical activity in midlife.

In concurrence with our aims and objectives this study has highlighted that physically active midlife will prevent or delay the onset of dementia in later life and this study has been unique in categorizing the patients into risk categories and comparing them with the controls.

Recommendation:

Future studies are required to evaluate whether physical activity can be used as a treatment modality to improve the quality of life of dementia patients. Studies with a larger sample size, a prospective study design and multicentric model would throw more light on the relation between physical activity and Dementia.

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