ORIGINAL ARTICLE

ROLE OF SOCIO-DEMOGRAPHY, LIFESTYLE AND COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) ON COGNITION IN PARKINSON DISEASE (PD) – A CROSS-SECTIONAL STUDY.

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Abstract

Objective: To study the role of socio-demography, lifestyle factors and the usage of complementary and alternative medicine (CAM) on cognition in Parkinson's disease. (PD)
The study was an observational, cross sectional study and was conducted at Perak Parkinson's Association Centre (PPA) and neurology clinic of Hospital Raja Permaisuri Bainun (HRPB).
A total of 51 patients, 14 patients from PPA and 37 patients from HRPB who were diagnosed with PD were included in the study. Patients were tested by Mini-Mental State Examination (MMSE) and face to face interview using a structured questionnaire.

Results: Patients who were in younger age group (< 60 years old) had better MMSE score compared to others (p=0.07). Those who attained at least secondary level of education were found to be at lower risk of cognitive impairment (p=0.047). Those with younger age of onset of PD (20-44 years old) had less risk of cognitive impairment (p=0.048). Duration of PD (p=0.040), use of traditional Chinese medicine (TCM) (p=0.009) and practice of Tai Chi (p=0.04) also had significant association with cognition.

Conclusion: Higher education level, younger age group, younger age of onset, duration of PD, use of TCM and practice of Tai Chi has significant association with cognition in PD patients. Further studies are needed to corroborate our findings.

Keywords: Parkinson's disease, cognition, demography, lifestyle, complementary and alternative medicines (CAM)

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder that develops gradually and characterized by resting tremor, bradykinesia and muscle rigidity.[1] People with PD would actually face these symptoms in the later stage of the disease mainly due to the loss of nigrostriatal cell and presence of Lewy bodies, which are intracellular alpha-synuclein positive inclusions.[2] PD could be made more complicated by non-motor symptoms (NMS) such as olfactory dysfunction, sleep disturbances, constipation, neuropsychiatric disorders and cognition problem.[3] The cognitive function in PD patients could be impaired resulting in dementia usually during advanced stage of the disease.[4] But cognitive impairment, which includes working memory, attention shift and visuospatial dysfunction, could present even in the early stages of PD. [5, 6, 7]

In later stages of PD, the severity of cognitive deficits would be more advanced.[2] This causes decline in their thinking and ability to reason which usually happens at least a year after their diagnosis.[8] Progressive cognitive impairment among the patients may not interfere with their daily life in early stage. However, with passage of time, increasing cognitive decline could reduce their quality of life.

The main culprit of PD is still unidentifiable. However few theories proposed that a combination of age, genetic and non-genetic factors could be responsible for diagnosis of PD.[2] Genetically, those who have history of PD in the family has 3 to 4 fold higher risk to develop the disease compared to those who do not have family history.[9] However, the complete mechanism of PD is still not known and some of the cases are usually rare in nature. Apart from this, few studies discover that PD occurs more commonly among male patients, especially those in older age groups. It is believed that the exposure to estrogens can serve as a neuroprotective effects in female patients [10] whereas the older onset PD has a faster progression compared to the younger onset with a shorter time span of the disease.[11]

Lifestyle of a PD patient could also affect the progress of cognitive decline. Generally, exercise and balanced diet is encouraged for everyone in order to promote healthy lifestyle. There is evidence that vigorous physical activity may have neuroprotective effect in PD and therefore it is advisable for the patients to maintain a healthy lifestyle.[12] Extensive research on the effect of nicotine in smoking has found out several controversial results. It is said that cigarette smoke can help to enhance dopamine release, stop the free radical damage to nigral cells through carbon monoxide [4] and inhibit monoamine oxidase B thus help fighting against toxic neuronal damage.[13] However, there are also evidence where smoking could increase the risk of dementia in PD by almost two fold.[14] Higher level of alcohol consumption on daily basis will significantly increase the risk of PD too.[15]

Several research studies have been done to see how complementary and alternative medicine could affect Parkinson's disease and some of them have shown positive benefit. For instance, music therapy has been used to promote movement and expression and have the ability to impact cognition and social function [16] In addition, herbal remedies are also used as some of these herbs could have beneficial effects on PD. A study conducted in Singapore found out that those who consume curry occasionally had better Mini Mental State Examination (MMSE) score in comparison to those rarely consumes curry.[17] It is believed that coconut oil acts as an alternative source of energy that is capable of stopping progressive neuronal death that could lead to dementia.[18]

PD could be associated with some life style related comorbid conditions for example hypertension, hyperlipidemia and diabetes. Hypertension and hyperlipidemia are few conditions which can cause decline in attention, recollection of memory, ability to process information and executive functions.[19] The risk

of PD is seen higher in patients with diabetes mellitus too.[20] This may be due to neurodegeneration that occurs when metabolic disruption affect the hippocampal area that is responsible for memory recall.

Generally, most of the studies done on PD are carried out to find more regarding the motor symptoms. There are very few studies that emphasize on the factors that could either maintain or cause further decline in cognitive function among PD patients.

Therefore, the objective of this research is to study the role of socio-demography, lifestyle factors and use of complementary and alternative medicine (CAM) on cognition in PD. Being able to address these factors could be very useful for early intervention among the patients. They could improve their quality of life if they get the necessary treatment thus reducing the progress of cognitive decline and risk of morbidity and mortality.

Methods

This was an observational, cross-sectional study conducted at neurology and medical clinics of Hospital Raja Permaisuri Bainun (HRPB), Ipoh and Perak Parkinson's Association Centre (PPAC), Ipoh, Perak, Malaysia. The study period was from 19th of March till 7th of April. Universal sampling method was used and all Malaysian patients suffering from idiopathic PD and aged 40 to 85 years ($\geqslant$40 to $\leqslant$85) and having ability to converse either in English or Bahasa Melayu were included in the study. In the case of illiterate patients, an impartial witness preferably the caregiver or one of the family members explained the contents of participant's information sheet orally to the subject. Individuals diagnosed with dementia, other neurodegenerative disorders (as diagnosed by neurologists), with dysphasia, secondary-parkinsonism, Parkinson-like syndrome and parkinsonism-plus syndromes, severe debilitating illness and individuals who refused to take part in the study were excluded.

The patients were interviewed by pre-validated structured questionnaire and MMSE. The interview was conducted and the data was collected by face-to-face interview by the trained researchers. MMSE was done on each patient, testing five areas of cognitive function, namely orientation, registration, attention and calculation, recall and language using patient's preferred language. Each patient was devoted about 30 minutes for collecting the data and conducting the MMSE. According to an article published by Korean Movement Disorder Society, MMSE can be used as a screening test for dementia in patients with Parkinson's disease, regardless of their educational level.[19] Subjects will be grouped into 4 groups according to MMSE score i.e., no cognitive impairment (MMSE Score 24-30), mild cognitive impairment (MMSE Score 21-23), moderate cognitive impairment (MMSE score 10-20) and severe cognitive impairment (MMSE Score 0-9). MMSE score for each patient was obtained by using either an English version according to the method prescribed by Folstein MF et al.[20] or Malay version as prescribed by Ibrahim NM et al.[21]

Statistical Package for Social Science (SPSS) version 21 was used for statistical analysis and $p<0.05$ was considered statistically significant. Descriptive statistics were presented with mean, standard deviation, median, interquartile range for continuous variables based on normality. Frequency with percentage was presented for categorical variable.

The study was conducted after obtaining ethical clearance from ethical committee of University Kuala Lumpur Royal College of Medicine Perak. Research was registered with the National Medical Research Registry (NMRR) for ethical approval from Malaysian Research Ethics Committee (MREC). Approval for data collection was obtained from the Hospital Director and Head of Department of Neurology and Perak Parkinson's Association. Written informed consent was obtained from each respondent after

explaining about the nature of the research and the patient could withdraw from the study at any time. All information collected from the participants are kept strictly confidential.

Results:

Table 1: Comparative Data of PD Patient With or Without Cognitive Impairment

	Frequency (*n*)	Percent (%)	Mean
No Cognitive Function Impairment (MMSE Score ≥ 24)	32	62.7	27
Impaired Cognitive Function (MMSE Score < 24)	19	37.3	18
Total	51	100.0	23.71

Table 2: Total Number of PD Patient and MMSE Score

MMSE Score	Frequency (n)	Percent (%)
24-30	32	62.7
21-23	6	11.8
10-20	12	23.5
1-9	1	2.0
Total	51	100

Table 3: Association between demography and MMSE scores.

Variables	No 24-30		Cognitive Impairment			Total	*p*-value
			Mild 21-23	Moderate 10-20	Severe <10		
	n	%	*n*(%)	*n*(%)	*n*(%)	%	
Age (years)							
Below 50	4	7.8	0	0	0	0	0.017*
50-59	7	13.7	0	0	0	0	
60-69	12	23.5	1 (2.0)	6 (11.8)	0	7 (13.7)	
70-79	9	17.6	3 (5.9)	4 (7.8)	0	7(13.7)	
80and above	0	0	2 (3.9)	2 (3.9)	1 (2.0)	5(9.8)	
Gender							
Male	22	43.1	2 (3.9)	7(13.7)	1(2.0)	10(19.6)	0.333
Female	10	21.6	4(7.8)	5(9.8)	0	9(17.6)	
Ethnicity							
Malays	8	15.7	0	1(2.0)	0	1(2.0)	0.092
Chinese	16	31.4	6(11.8)	4(7.8)	0	10(19.6)	
Indian	7	13.7	0	7(13.7)	1(2.0)	8(15.7)	
Others	1	2.0	0	0	0		
Educational level							
None	3	5.9	0	5(9.8)	0	5(9.8)	0.047*
Primary level	6	11.8	3(5.9)	5(9.8)	0	8(15.7)	
Secondary level	17	33.3	3(5.9)	2(3.9)	1(2.0)	6(11.8)	
College or university level	6	11.8	0	0	0	0	
Occupation							
Self employed	4	7.8	0	1(2.0)	0	1(2.0)	0.696
Unemployed	18	35.3	6(11.8)	9	1(2.0)	16(31.4)	
Government	4	7.8	0	0	0	0	
Private	6	11.8	0	2(3.9)	0	2(3.9)	
Income (RM)							
1000 and below	5	9.8	2(3.9)	4(7.8)	0	5(9.8)	0.657
1001- 3000	19	37.3	2(3.9)	7(13.7)	1(2.0)	10(19.6)	
3001.00-5000.00	6	11.8	2(3.9)	0	0	2(3.9)	
>5000.00	2	3.9	0	1(2.0)	0	1(2.0)	

*statistically significant: *p*-value<0.05

Table 4: Association between clinical characteristics and MMSE scores.

Variables	No		Cognitive Impairment				*p*-value
	24-30		Mild	Moderate	Severe	Total	
			21-23	10-20	<10		
	n	%	*n*(%)	*n*(%)	*n*(%)	n(%)	
Family History of PD or Alzheimer's disease (AD)							
Yes	8	15.7	1(2.0)	1(2.0)	0	2(3.9)	0.607
No	24	47.1	5(9.8)	11(21.6)	1(2.0)	17(33.3)	
Age at onset of PD							
20-44 years old	7	13.7	0	0	0	0	0.048*
45-64 years old	14	27.5	0	6(11.8)	0	6(6.1)	
65 years old and above	11	21.6	6(11.8)	6(11.8)	1(2.0)	13(25.5)	
Duration of PD							
Less than 1 year	2	3.9	1(2.0)	0	1(2.0)	2(3.9)	0.040*
1-5 years	15	29.4	4(7.8)	7(13.7)	0	11(21.6)	
6-10 years	10	19.6	1(2.0)	5(9.8)	0	6(6.1)	
More than 10 years	5	9.8	0	0	0	0	
Caregiver							
No	2	3.9	0	0	0	2(3.9)	0.744
Yes	30	58.8	6(11.8)	12(23.5)	1(2.0)	19(37.3)	
Comorbid Conditions							
None	14	27.4	2(3.9)	3(5.9)	0	5(9.8)	0.576
Hypertension	6	11.8	1(2.0)	3(5.9)	1(2.0)	5(9.8)	0.556
Diabetes mellitus	5	9.8	1(2.0)	6(11.8)	0	7(13.7)	0.182
Hypercholesterolemia	9	17.6	2(3.9)	4(7.8)	1(2.0)	7(13.7)	0.774
Coronary artery disease	2	3.9	1(2.0)	0	0	1(2.0)	0.523
Arthritis	1	2.0	0	1(2.0)	0	1(2.0)	0.871
Others	5	9.8	3(5.9)	3(5.9)	0	6(11.8)	0.284

*statistically significant: p-value<0.05

Table 5: Association between lifestyle and MMSE scores**.**

Variables	No 24-30		Cognitive Impairment				*p*-value
			Mild 21-23	Moderate 10-20	Severe <10	Total	
	n	%	*n* (%)	*n* (%)	*n* (%)	*n* (%)	
Smoking							
No	22	43.1	5(9.8)	8(15.7)	1(2.0)	14(27.5)	0.697
Current smoker	4	7.8	0	0	0	0	
Former smoker	6	11.8	1(2.0)	4(7.8)	0	5(9.8)	
Alcohol consumption							
No	26	51.0	4(7.8)	8(15.7)	1(2.0)	13(25.5)	0.619
Occasionally	6	11.8	2(3.9)	3(5.9)	0	5(9.8)	
Less than once daily	0	0	0	0	0	0	
At least once daily	0	0	0	1(2.0)	0	1(2.0)	
Fitness activities							
No	6	11.8	0	4(7.8)	1(2.0)	5(9.8)	0.150
Often	21	41.2	5(9.8)	4(7.8)	0	9(17.6)	
Sometimes	5	9.8	1(2.0)	4(7.8)	0	5(9.8)	
Social and productive activities							
No	15	29.4	2(3.9)	8(15.7)	1(2.0)	11(21.6)	0.638
Often	15	29.4	4(7.8)	3(5.9)	0	7(13.7)	
Sometimes	2	3.9	0	1(2.0)	0	1(2.0)	
Dietary Practice							
Low carbohydrate	2	3.9	1(2.0)	1(2.0)	0	2(3.9)	0.739
Low fat	0	0	0	1(2.0)	0	1(2.0)	0.346
Low protein	2	3.9	0	1(2.0)	0	1(2.0)	0.902
Vegetarian	2	3.9	0	0	0	0	0.744
Vegan	2	3.9	0	0	0	0	0.744
Others	0	0	1(2.0)	1(2.0)	0	2(3.9)	0.208

*statistically significant: *p*-value<0.05

Table 6: Association between CAM, coconut oil and curcumin and MMSE score

Variables	No 24-30		Cognitive Impairment				*p*-value
			Mild 21-23	Moderate 10-20	Severe <10	Total	
	n	%	*n*(%)	*n*(%)	*n*(%)	*n*(%)	
Complementary and Alternative Medicine (CAM) Usage							
Traditional Chinese medicine	2	2.0	3(2.9)	2(2.0)	0	5(4.9)	0.009*
Ayurvedic medicine	1	1.0	0	0	0	0(1.0)	0.774
Traditional Malay medicine	3	2.9	0	1(1.0)	0	1(1.0)	0.760
Herbs	5	4.9	2(2.0)	1(1.0)	0	3(2.9)	0.345
Vitamin or supplements	24	23.5	4(3.9)	8(7.8)	0	12(11.8)	0.100
Chiropractic, therapeutic and osteopathic	1	1.0	1(1.0)	0	0	1(1.0)	0.183
Meditation	4	3.9	0	0	0	0	0.334
Prayer	10	9.8	1(1.0)	3(2.9)	0	4(3.9)	0.834
Yoga	3	2.9	0	0	0	0	0.448
Tai Chi	7	6.9	4(3.9)	3(2.9)	0	7(6.9)	0.04*
Relaxation	5	4.9	0	0	0		0.245
Art, dance and music therapy	3	2.9	0	1(1.0)	0	1(1.0)	0.760
Coconut oil consumption							
None	18	35.3	6	7(11.8)	0	13(25.5)	0.633
Rarely	3	5.9	0	0	0	0	
Occasionally	1	2.0	0	1(2.0)	0	1(2.0)	
Often	3	5.9	0	1(2.0)	0	1(2.0)	
Very often	7	13.7	0	3(5.9)	1(2.0)	4(3.9)	
Curcumin consumption							
None	11	21.6	1(2.0)	1(2.0)	0	2(3.9)	0.713
Rarely	2	3.9	1(2.0)	1(2.0)	0	2(3.9)	
Occasionally	5	9.8	0	2(3.9)	0	2(3.9)	
Often	8	15.7	2(3.9)	3(5.9)	0	5(9.8)	
Very often	6	11.8	2(3.9)	5(9.8)	1(2.0)	8(15.7)	

*statistically significant: *p*-value<0.05

Table 7: Complementary and Alternative Medicine (CAM) Users and Cognition

		No Cognitive Function Impairment		Impaired Cognitive Function		
		n	%	*n*	%	p-value
Complementary and Alternative Medicine	No	2	33.3%	4	66.7%	0.031
	Yes	30	66.7%	15	33.3%	

Discussion

Cognitive function enables us to think, reason, store memories and even process information. Although cognitive change is considered as a normal process of aging, it is known that PD could cause cognitive impairment even at a different rate and different pace compared to those without PD. Therefore it is necessary to identify possible risk or protective factors to help prevent cognitive impairment in PD patients. This study explored and determined a few findings, which could be associated with cognition in PD patients.

Advancing age is one of the well-known risk factor for causing a decline in cognitive function in PD and many studies reveal that those who are older are more prone to have cognitive impairment and develop dementia.[14, 24] This is also observed in our study and patients in younger age group have normal cognitive function in comparison to those in older age group. There are evidences from a few neuropathological studies that there is a strong association between the deposition of cortical amyloid- β as found in PD and also aging with the later diagnosis of dementia.[25] There are also studies linking between the age-related increase of Lewy bodies and also Parkinson's disease Dementia (PDD).[26, 27] These age-related neuropathological processes occurring over time may increase the likelihood of the PD advancing into PDD.

Duration of the disease is also a significant aspect and according to previous studies, longer duration of disease is said to cause an increase in the risk of cognitive decline.[28, 29] But, our study found out that those who have been diagnosed with PD for more than 10 years have normal cognition. This could be correlated to other factors. For instance, all five patients actually had education level of at least a secondary level, practiced at least one type of complementary and alternative medicine and also engaged in fitness activity at least once a day. Besides that, four out of five of them actually had an early onset of the disease i.e. before 50 years of age. These few factors could be possible reasons why they have normal cognition despite the longer duration of disease. In our study, the age of onset of PD reveals a correlation to cognitive impairment. There was no cognitive impairment among patients who had early onset of the disease (20-44 years old) in comparison to those who developed PD at later age. This is in consistence with another study where it was reported that those who had an older onset of PD had poorer cognition and faster progression of the disease.[30, 31]

In addition to this, educational level had shown close interrelation to cognition. It is likely that higher educational level has a protective effect against deterioration in cognition. Patients who

attained secondary and tertiary education actually performed better MMSE score. This is further supported by previous studies, which observe that higher educational level provides the patients with better understanding of the disease process, which could delay the progress of PD.[32, 33] Therefore, greater emphasis should be put in explaining the disease process, complications, beneficial effects of the drugs, lifestyle, etc. which may be helpful in preserving the cognition among PD patients.

Based on our study, the practice of complementary and alternative medicine (CAM) has correlation with cognitive function among PD patients (p=0.028). Among 45 of the patients who are practicing CAM, 68.9% of them had normal cognitive function. Traditional Chinese medicine (TCM) and also Tai Chi show significant association with cognitive function. However, definite conclusion cannot be done due to very small sample size. Results from a few studies indicated that those who practiced Tai Chi had better cognition.[34,35] Tai Chi not only improves the body's balance, but it also aids to improve the visual attention in the elderly. Therefore, applying Tai Chi as an exercise actually could be a great help as it not only keep the patients healthy but also improve their memory. Traditional Chinese Medicine (TCM) has long been used in PD and is thought to have neuroprotective effect and slow down the progress of the disease and improve both motor and non-motor symptoms. [34, 35] However, in our study, only 7 patients were using TCM out of which 2 were having normal cognitive function and 5 were having different degree of CI. Therefore, we cannot draw any conclusion from our study because of small sample size.

We did not find any association of gender and ethnicity with cognitive function in PD patients which corroborated with another study done in Malaysia.[11] However, there were earlier researches where male gender was found to be a risk factor for PD. [10,14]

Based on our study, patient's current occupation and also household income had no correlation with cognitive function too.

Our study did not find any association between fitness activity and cognition despite existing studies having evidence that vigorous physical activity may have neuroprotective effect in PD. [36] Similarly, we did not observe any association of social and productive activities with cognition. This could again be due to our small sample size. Smoking and alcohol consumption also had no link with cognitive function based on our study, even though both these factors were thought to cause a decrease in cognition as evident by other study. [37]

Our study did not find any association between the different types of diet practices and cognitive function. Nutrition actually plays a role in ensuring a healthy lifestyle among us all. There are nutrients that could either be neuroprotective or increase the likelihood of PD. However, fat, meat and carbohydrates have conflicting results on whether they could either promote neuroprotection or neurodegeneration.[38] More studies are needed to establish better findings regarding this aspect. Additionally, both coconut oil and curcumin had no significant correlation with cognition in our study, despite the claim both having neuroprotective factor against PD. [17, 18]

Our study found no association between comorbid conditions such as diabetes and hypertension with level of cognition. This is consistent with a meta-analysis done in 2011 which found out inconclusive evidence that could suggest diabetes to be a risk factor of PD. [39] There is also no significant association between quality of life of PD patients and cognitive function based on our study. It is important to maintain the quality of life among the patients so that they could still feel the sense of independent living despite their condition. Better mental status and mood will ensure better maintenance of physical health among PD patients.[40]

Limitations

One of the limitations while conducting this research was the difficulty in finding patients with PD in such a short period of time. Although we recruited patients from the neurology clinic of HRPB and also PPA, we could only get 51 patients, which was a very small sample size. The possibilities of bias could not be eliminated as the data obtained by questionnaires were self-reported by the patients.

Conflicts: The authors declare no conflict of interest.

Conclusion

Our study concludes that different factors like younger age group, younger age of onset, higher educational level, and duration of PD, use of TCM and practice of Tai Chi can affect cognitive function among PD patients. However, further studies with larger sample size are needed to establish our findings.

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