

Risk factors for development of dementia in Parkinson's disease: Effect of family history

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ABSTRACT

Background: Parkinson's disease is one of the most common neurodegenerative disease characterized by tremors at rest, rigidity and akinesia. Despite being one of the common neurodegenerative diseases etiology and progression of PD is complex and poorly understood and has proposed to be a combination of genetic and environmental factors. Nearly 80% of the patients of Parkinson's disease go on to develop dementia. However, there are considerable variations in disease course and some patients develop dementia quite early in the disease course. The genetic factors and association of family history for early development of dementia is still something that is controversial and under study. This study is an attempt to understand the significance of family history in development of dementia in Parkinson's disease.

Patients and methods: This cross-sectional comparative study was conducted in Sheikh Zayed Postgraduate Medical Institute Lahore in which participants were assessed for dementia through Mini mental state examination. The subjects were divided in three groups of 30 each - Parkinson's disease with dementia group, Parkinson's disease without dementia group and a healthy control group and a potential association between family history of dementia and development of dementia in Parkinson's disease was studied.

Results: Out of total 90 patients, 23 (25.6%) had a family history of Parkinson's disease in Group A (Parkinson's disease with dementia), 9 (30.0%) patients in Group B (Parkinson's disease without dementia) whereas in healthy controls only 5 (16.7%) patients had family history of Parkinson's disease. Chi-square test revealed that the difference in the proportion of family history of Parkinson's disease among the groups was insignificant (p-value = 0.393).

Conclusion: No associations between dementia in PD and familial occurrence of dementia could be established. A longitudinal cohort study performing cross sections at intervals would be valuable to further study the effect of family history and early signs of dementia in patients of Parkinson's disease.

Keywords:

Parkinson's Disease; Dementia; Family History

INTRODUCTION

Parkinson's disease (PD) is also known as Paralysis Agitans. It is the second most common neurodegenerative disease with 1-2 cases per 1000 of the population at any one time. About 1.5% of the population above the age of 65 years suffers from Parkinson's disease.¹ The diagnosis and monitoring of is dependent entirely on clinical parameters as no disease biomarker has been identified so far.² The pathogenesis leading to neurodegeneration is not yet fully clear, only certain risk factors have been identified. Parkinson's disease is characterized by a large number of both motor and non-motor features. Among the non-motor symptoms, dementia has the biggest impact on the quality of life of the affected individual.³ The risk of

dementia in patients with Parkinson's disease is substantial with a point prevalence close to 30%.⁴ Dementia in Parkinson's disease positively correlates with increasing age. The prevalence of dementia in Parkinson's disease is often overlooked by the neurologists resulting in a late diagnosis, often coming to notice only after serious cognitive impairment has already taken place. Dementia and the accompanying cognitive decline is associated not only with increased mortality and morbidity but also creates a strain on caregivers and health system. Therefore, the risk of developing dementia in PD is often an important topic for patients, their families and health professionals.^{5,6} Previously, environmental and social factors were implicated as a possible risk factors for PD but in the last two decades heritability has also come forward as a significant risk factor. A family history of PD in first degree relatives is found in approximately 15% of the patients. In young onset cases, the risk is even higher with a family history of 25.5%.^{7,8}

Conflict of interest: The authors declared no conflict of interest exists.

Citation: Kazmi T, Nasir A, Anwar M, Mahmud Q, Anwar W, Rao M. Risk factors for development of dementia in Parkinson's disease: Effect of family history. J Fatima Jinnah Med Univ. 2020; 14(x): 191-194.

DOI: <https://doi.org/10.37018/uuqo3691>

The genetic factor for development of dementia in Parkinson's disease has still not been established but the few studies that were done do point towards a positive family history of dementia being a risk factor. Familial inheritance and genetic transmission have emerged as an indicator for development of Parkinson Disease Dementia^{9,10} Most of the data available on Parkinson's disease and dementia has been collected from the west and cannot be applied to South Asian population because of differing epidemiological factors.

PATIENTS AND METHODS

A cross-sectional comparative study design was employed and the study was conducted in Physiology Department of Sheikh Zayed Postgraduate Medical Institute in collaboration with Sheikh Zayed hospital Neurology Department. This study was conducted from September 2014 till February 2015. A population of 90 age and gender matched subjects was chosen. The study included clinically diagnosed patients of Parkinson's disease with and without dementia and healthy controls all above the age of 50 yrs.. Subjects with brain tumor, pituitary disease and cerebral lesions were excluded from the study. The subjects were distributed into three groups: Group A comprising 30 patients of PD with dementia, Group B comprising 30 patients of PD without dementia and Group C including 30 healthy controls. The mean age of group A was 63.9 ± 5.7 , mean age of group B was 62.6 ± 5.6 and mean age of group C was 61.6 ± 5.1 . The mean difference in age among all the groups was insignificant (p-value = 0.266).

Every individual was assessed by taking history and using Mini Mental state examination (MMSE). MMSE is a 30 point questionnaire test of cognition that is commonly used in medicine and allied health to screen for dementia as well as in research setting to measure cognitive impairment. It requires no special equipment and training and can be performed in five to ten minutes. A score of 24 or more (out of 30) indicates a normal cognition. Scores less than 24 indicate cognitive impairment and possible dementia with lesser scores indicating a higher degree of cognitive decline. We,

however, assessed for only presence or absence of cognitive impairment.. The data was analyzed using SPSS version 20. Mean \pm SD and median with inter-quartile range was given for quantitative variables i.e., age, body mass index and MMSE score. Frequency and percentage were given for family history of dementia and PD. Shapiro Wilk test was used to check the normality of data. For not normally distributed data non parametric Kruskal Wallis test and for normally distributed data one-way ANOVA test was used to compare the mean difference in quantitative variables among groups. Chi square / Fisher's exact test was to determine the association of history of family history of dementia and Parkinson's disease with the groups. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Subjects were selected from both inpatient and outpatient department of Sheikh Zayed Medical complex meeting the inclusion and exclusion criteria. The study was conducted on 90 participants. Of these, 30 participants had Parkinson's disease with dementia, 30 had Parkinson's disease without dementia and 30 were healthy controls.

The mean age of group A was 63.9 ± 5.7 , mean age of group B was 62.6 ± 5.6 and mean age of group C was 61.6 ± 5.1 . The mean difference in age among all the groups was insignificant (p-value = 0.266).

When family history of Parkinson's disease was compared in group A and B, it was revealed that both the groups had an equal percentage of positive family history i.e., 70% as shown in Table 2. Similarly, percentage of family history of dementia was also comparable in three groups with values of 83.3%, 86.7% and 100% in groups A, B & C respectively, with the p-value of 0.075, as shown in Table 3. Out of total 90 subjects, 9 (10.0%) had a family history of dementia. In group A, 5 (16.7%) and in group B, 4 (13.3%) patients had family history of dementia whereas in group C no subject had a family history of dementia. Fisher's exact test revealed that the difference in the proportion of family history of dementia among all the groups was insignificant (p-value= 0.072)

Table 1. Distribution of Participants in three groups by Age

	Mean \pm SD	Minimum	Maximum	p-value
Group A	63.9 ± 5.7	56	74	0.266
Group B	62.6 ± 5.6	55	75	
Group C	61.6 ± 5.1	55	70	

Table 2. Frequency of family history of Parkinson's disease among the groups

Group	Family History of Parkinson's disease		Total
	No n (%)	Yes n (%)	
Group A	9 (30.0%)	21 (70.0%)	30 (100%)
Group B	9 (30.0%)	21 (70.0%)	30 (100%)
Group C	5 (16.7%)	25 (83.3%)	30 (100%)
p-value	0.393		

Table 3. Frequency of family history of Dementia

Group	Family History of Dementia		Total
	No n (%)	Yes n (%)	
Group A	5 (16.7%)	25 (83.3%)	30 (100%)
Group B	4 (13.3%)	26 (86.7%)	30 (100%)
Group C	0 (0.0%)	30 (100.0%)	30 (100%)
p-value	0.075		

DISCUSSION

In this study association was evaluated between family history of Parkinson's disease, family history of dementia and whether positive family history of either of these had a positive correlation with early development of dementia in patients of Parkinson's disease. In this study the mean age of patients with PD with dementia was 63.9 ± 5.7 years, mean age of Parkinson's disease without dementia was 62.6 ± 5.6 yrs and that of healthy controls was 61.6 ± 5 years. Birju and coworkers pointed out that cognitive abilities reach a plateau in 50 and 60 years and decline in 70 years.¹¹ Another study conducted by Harada and colleagues stated that peak of cognitive abilities is at 30 years of age with a decline thereafter.¹² Murman and coauthors also described the increasing frequency of people with age related neurodegenerative dementia.¹³ So while age is a proven determinant of cognitive decline, in our study age difference between the three groups was insignificant ($p = 0.266$) and can be ruled out as a contributing factor towards low MMSE scores.

Out of total 90 subjects, 23 (25.6%) had a family history of Parkinson's disease in Group A, 9 patients in Group B (30.0%) where in Group C only 5 (16.7%) patients had family history of PD. No statistical significance was established for the difference in the proportion of family history of Parkinson's disease among the groups was insignificant ($p=0.393$). This correlates well with previous studies which showed no association between positive family history for dementia or PDD.¹⁴⁻¹⁶ Rosen and group showed a positive association between risk of development of PD and the family history of Alzheimer's disease and Parkinson's disease.¹⁷ However, this study did not make segregation between cognitive decline due to Alzheimer's and Parkinson's disease. Out of total 90 subjects in this study, 9 (10.0%) had a family history of dementia. In

group A, 5 (16.7%) and in group B, 4 (13.3%) patients had family history of dementia whereas in group C no subject had a family history of dementia. This study failed to show any significant association between family history of dementia and development of dementia amongst subjects ($p = 0.075$). Previous researchers suggested in their studies that parental history of dementia lead to a higher prevalence of dementia in off springs.^{18,19} Another study showed a positive association between family history and development of dementia.²⁰ However, the sample size in this case was small and the population under study was only patients of Alzheimer's dementia. An interesting finding came up in a study done by Roca and colleagues showing a significantly increased risk of development of dementia in first degree relatives of patients of Parkinson's disease which may point out some genetic component associated with Parkinson's disease and mild cognitive impairment. In this population-based sample, the risk of cognitive impairment or dementia was modestly increased overall but was sizably increased for relatives of patients with younger age at onset of PD. This study was different from conventional studies because it assessed relatives individually rather than just taking family history.²¹

CONCLUSION

No associations between dementia in Parkinson's disease and family history of dementia could be established. Further studies with larger sample size are needed to explore a possible relationship between a family history of Parkinson's Disease and development of dementia in Parkinson's Disease and its potential pathophysiology.

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