Prevalence rate corresponding to signs/Symptoms and Risk Factors of Parkinson's disease Patients in District Abbottabad, Khyber Pakhtunkhwa, Pakistan

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Parkinson's disease (PD) is a well famous neurological disorder associated with diminished functioning of dopamine-producing neuronic cells located in the substantia nigra of the midbrain. Clinically PD indicates dual motor and non-motor signs and symptoms. The frequently noticed non-motor symptoms included sadness, anxiety, sleep disorder, mood disruption, memory issues, and sleep disorder. In contrast, the motor symptoms included sluggish walking, patronized posture, resting tremors, and muscle stiffness. The current study aimed to examine the prevalence of signs/symptoms and risk factors linked to PD progression in both male and female subjects of district Abbottabad, Khyber Pakhtunkhwa, Pakistan. In a current study previously diagnosed PD patients were included. A well-defined standard questionnaire was used to be filled out by the patients who visited different hospitals (both public and private sectors) of district Abbottabad. Collected data was analyzed using SPSS version 20. According to the findings, a high prevalence rate of PD was observed in males (86.2%) than females (13.7%) candidates. Moreover, PD cases were sporadic, with greater prevalence observed in patients above 50 years of age. Similarly, about 88.2% of patients indicated disease occurrence at a later age or late onset. Accordingly, numerous factors including occupation, education level, head injury, pesticide exposure, and anxiety might play an essential role in the progression of PD, in addition to gender and age. The NMS such as anxiety, memory issues, feeling sad or blue, difficulty in walking, sleeping problems, and micrographia were noticed as the most prominent risk factors associated with PD development in patients of the district Abbottabad. Awareness regarding PD in the People of district Abbottabad needs to be enhanced since most of the residents have the wrong perception that aging-associated weakness is the underlying cause of PD. Different scientific communities' particularly governmental and social welfare sectors and community pharmacists might play an important role in the prevention of disease progression in District Abbottabad and other nearby districts of KPK Pakistan.

Keywords: Parkinson's disorder, Pakistan, KPK, Risk factors, NMS

Authors Summary:

Muhammad Fawad Khan collected and compiled the data. Dr. Aamna shah supervised the students are completed their work. Tasneem Noor Muhammad and Hafeezullah Wazir Ali facilitated the student in data collection and facilitated him in any additional guidelines

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required. Nargis Aman, Shoaib Nawaz, and Bilal Haroon helped in thesis and paper writing. This paper aims to examine the prevalence of sign/symptoms and risk factors linked to PD progression in both male and female subjects of district Abbottabad, Khyber Pakhtunkhwa, Pakistan, and to provide awareness regarding PD in the district Abbottabad population, needs to be enhanced, since most of the residents have the wrong perception that aging-associated weakness is the underlying cause of PD. Different scientific communities' particularly governmental and social welfare sectors and community pharmacists might play an important role in the prevention of disease progression in District Abbottabad and other nearby districts of KPK Pakistan. Current research might be helpful at the international level to reduce occurrence and occurrence of parkinsonism increase cost burden on ultimate consumers. Current study might be implemented at hospital and community levels to enhance disease awareness and ways of progressing mental health.

Introduction

James Parkinson in early 1817 initially described shaking palsy as a disorder manifested by degenerative conditions of the central nervous system [1]. PD is the second most frequently reported neurological disorder classified under malfunctioning or abnormal body movements [2]. PD is associated with the sequential depletion of dopamine and other associated neurotransmitters and is perceived via particular signs and symptoms, including bradykinesia (slowness of movement), stiffness (limbs and trunk rigidity), postural instability (difficulty moving), and tremors or shaking of numerous body parts. Harm to about 60–80% or more of its dopamine-releasing cells within the cranial substantia nigra damage may result in the observation of aforementioned symptoms [1-2]. Epidemiological review ascribes the existence of PD in around 1-2 people out of 1000 with at least 1% of the population in the age limit above 60 years [3]. Thus persistence of PD symptoms is mostly frequently associated with an elderly or aged population. Neuropsychiatric disorders, autonomic manifestations, sensory malfunctioning, sleep disorders, and exhaustion are the most common non-motor symptoms (NMS) experienced by patients diagnosed with PD [4]. Approximately 90% of PD patients indicated NMS symptoms from the initial to advanced stages [5]. Poor survival rates and deprived living have been reported to be associated with NMS-associated PD [6]. PD NMS has commonly reported been by signs and symptoms including dementia, dysautonomia, sleep difficulty, depression with saliva dribbling, visual dysfunction, weight changes, and sex issues being less frequently reported [7]. Likewise, several NMSs, including apathy, bowel incontinence, sexual dysfunction, and sleep disruption, have not been reported to the attending doctors, particularly due to patients' unawareness or augmented comfort level of the patient in describing such symptoms to the medical practitioner [8]. The occurrence rate of PD pathogenesis is comparatively higher in male subjects as compared to females attributed to several intervening factors such as including toxicant exposure, head trauma, mitochondrial malfunction, neuro-protection, and X-linkage of genetic genes [15]. Similarly, overexpression of PD in male subjects might also be correlated to their frequent exposure to various environmental factors such as the utilization of well water, living in a rural area, and farming along with close contact with

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pesticides [16–17]. In contrast, studies conducted to explore the participation of Non-steroidal anti-inflammatory medications (NSAID), nicotine, corticosteroids, and statins role in PD progression indicated a negative impact of such components in PD progression [18–21]. The current study requires detailed analysis and to the best of our knowledge; the prevalence and potential risk factors involved in the prognosis of PD at district Abbottabad have not yet been established. The current study aimed to evaluate the analysis of symptoms and potential risk factors associated with PD development in patients in the district of Abbottabad.

Material and Method

Approval for the current study

Before initiation, the study was approved (approval number# 73/HU/ORIC/IBC/2016/1058) by the bioethical committee of Hazara University, Mansehra, Pakistan.

Area of population

After approval, the study was conducted in the district of Abbottabad, located in the southern region of the province of Khyber Pakhtunkhwa (KPK), Pakistan. The total population of district Abbottabad is approximately 57,525,047 people with a living area of about 1,167,892. The total included population was about 1,117,927 with the majority of participants from rural areas and some specific patients from urban areas (approximate population of 49,965) as well.

Study selection and organization

Well-structured and standardized questionnaire approved by Dr. George D. Mellick (Griffith University, Brisbane, Australia,) was utilized for the subtle assessment of PD patients. The questionnaire was compiled via a face-to-face interview with the PD patients. Six months' time duration i.e. from December 2018 to June 2019 was utilized for effective data collection including both the cases and control subjects. Data collection comprises a survey technique with PD patients from both the public sector hospitals and private clinics. All the patients with a confirmed clinical diagnosis of PD and control cases that fulfilled the inclusion criteria and belonged to various regions of district Abbottabad were included in the current study. Both PD patients and control group participants who expressed interest in active participation in the current study were included after taking signatures on appropriately written consent. 51 patients with confirmed diagnosis of PD were selected for inclusion in the current study with their complete personal and demographic information being collected either from direct conversation with the patients or their caregivers. As most of the patients were illiterate and unable to understand the questionnaire, therefore to fill the questionnaire; the interviewer asked questions in the local Pashto language.

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Statistical Evaluation

After a satisfactory review of collected data for accuracy and liability with reconfirmation and correctness of any information that may result in biases; the collected data was analyzed using SPSS (version 20). The chi-square test was applied separately on individual variables along with P-value determination to analyze the sequential matching of unadjusted odd ratios (OR) and corresponding confidence intervals (CI) of 95% were computed for individual putative risk factors. The multivariate analysis was performed on all risk factors that occurred in the study. A P-value of ≤ 0.05 was considered statistically significant in the current investigation.

Results

The current study identified 51 cases of PD with their detailed analysis from December 2018 to June 2019, however, the actual number of PD might be quite high attributed to the wrong perception of people of Abbottabad district that the current disorder is normally associated with aging factor along with possible negligence of its treatment. Among fifty-one participants, forty-four (86.2%) were male and seven (13.7%) were female. Epidemiological investigation on the incidence and prevalence of current disease in the district Abbottabad of KPK, Pakistan has not yet been described.

The results of descriptive statistical analysis associated with occupation, living status, history, and PD onset are presented in Table 1. According to the results, the prevalence of PD was significantly greater in labor (37.25%) and farmers (33.33%) respectively. Similarly, the occurrence of disorder was extremely prevalent in rural areas (98.11%) than in urban areas. About 50 cases (except a single case) suffered from sporadic PD with its onset mostly observed at a later age (above 40 years).

Table 1: Table indicating statistical analysis of numerous variables associated with PD patients.

Variables	Case (n= 51)	
	Yes	%
Occupation		
a) Farmer	17	33.33
b) Labor	19	37.25
c) Housewives	07	13.72
d) Govt. Servants	08	15.68
Living Status		
a) Urban region	03	05.88
b) Rural region	48	98.11
PD History		
a) Familial PD	1	01.96
b) Sporadic PD	50	98.03
Disease Onset		

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a) Late Onset	45	88.23
b) Young Onset	06	11.76

The results indicating the risk factors associated with PD patients are shown in Table 2. According to the results, the prevalence of disease was significantly higher in patients frequently exposed to pesticides i.e.17 cases (33.33%). Moreover, Tobacco users were more prone to PD i.e. 21 cases (41.17%) similarly patients that experienced head injuries also indicated a greater occurrence of PD disease (17 cases, 33.33%). According to the results several environmental risk factors, are strongly associated with the development of PD.

Table 2: Identification of various risk factors associated with progression of PD.

Variables	Case (n= 51)	
	Yes	%
Pesticide Exposure	17	33.33
Tobacco user	21	41.17
Head injury	17	33.33
Tea and coffee User	51	00
Anti-inflammatory Drugs		
a) Paracetamol User	11	21.56
b) Ibuprofen User	03	05.88
c) Aspirin User	10	19.60

The prevalence of motor and non-motor symptoms associated with PD patients is shown in Tables 3 and 4 respectively. According to the results resting tremors are the most frequent motor symptom observed in PD patients. Moreover, tremors are more commonly observed in female patients (100%) than male participants (92.4%). The main motor symptom of PD that greatly affects females (71.4%) than males (68.8%) is stiffness of the muscles.

Likewise, smaller handwriting (41 cases; 80.39%), loss of Interest (40 cases; 78.43%), memory issues (37 cases; 72.54%), Softer Voice (37 cases; 72.54%, and troubles arising from the chair (35 cases and 68.62%) respectively, were the most common NMS associated with PD. In the current study, the frequency of NMS in PD patients of district Abbottabad has been demonstrated for the first time. In general, all the patients (both male and female participants with percentages of 81.8% and 71.4% respectively) indicated the highest NMS prevalence rate for micrographia or smaller handwriting. Similarly, the presentation of slow movement issues in patients suffering from PD was more commonly experienced in male patients (88.7%) than in female patients (85.5%). A higher ratio of anxiety attacks has been expressed by the patients included in the current study with the anxiety ratio comparatively higher in males (72.7%) than female (57.4%) patients. While in our study, both male and female patients (85.5%) have serious memory issues. In the current study patients, observation of feeling faint, weak, or dizzy is a symptom of noticeable concern and was

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observed to be equally common in both male (72.7%) and female subjects (71.4%). Similarly, sleep issues, and feelings of helplessness and hopelessness, were noticed to be more prone in female individuals than male participants.

Table 3: Prevalence of motor symptoms associated with PD patients

Symptoms	All Patients	Male (n=44)	Female (n=7)	P values
Motor Symptoms				
a) Resting Shaking (tremor)	49 (96.07%)	42 (95.45%)	07 (100%)	0.56
b) Posture Instability	30 (58.82%)	24 (54.54%)	06 (85.71%)	0.12
c) Slow Walking	45 (88.23%)	39 (88.63%)	06 (85.71%)	0.82
d) Muscle Stiffness	35 (68.62%)	30 (68.18%)	05 (71.42%)	0.86

Table 4: Prevalence of non-motor symptoms associated with PD patients (Significance* level = p-value ≤ 0.05)

Symptoms	All Patients	Male (n=44)	Female (n=7)	p values
Non-Motor Symptoms				
a) Feeling Blue or Sad	26 (50.98%)	20 (45.45%)	06 (85.71%)	0.04*
b) Loss of Interest	40 (78.43%)	33 (75%)	07 (100%)	0.13
c) Sleep problem	31 (60.78%)	26 (59.09%)	05 (71.42%)	0.53
d) Memory problem	37 (72.54%)	31 (70.45%)	06 (85.71%)	0.40
e) Difficulty in buttoning the button	34 (66.66%)	29 (65.90%)	05 (71.42%)	0.77
f) Smaller handwriting	41 (80.39%)	36 (81.81%)	05 (71.42%)	0.09
g) Troubles arising from the chair	35 (68.62%)	28 (63.63%)	07 (100%)	0.05*
h) Softer Voice	37 (72.54%)	31 (70.45%)	06 (85.71%)	0.40
i) Poor Balance	30 (58.82%)	25 (56.81%)	05 (71.42%)	0.46
j) Less Expressive Face	33 (64.70%)	31 (70.45%)	05 (71.42%)	0.68
k) Hearing/Seeing things	20 (39.21%)	18 (40.90%)	02 (28.57%)	0.53
l) Anxiety illness	36 (70.58%)	32 (72.72%)	04 (57.14%)	0.40
m) Weakness/dizziness	37 (72.54%)	32 (72.72%)	05 (71.42%)	0.94
n) Hopelessness	18 (35.29%)	15 (34.09%)	03 (42.85%)	0.65
o) Frighten feeling	26 (50.98%)	21 (47.72%)	05 (71.42%)	0.24
p) Satisfactory life status	33 (64.70%)	28 (63.63%)	05 (71.42%)	0.65
q) Lack of Happiness in Life	23 (45.09%)	20 (45.45%)	03 (42.85%)	0.89
r) Unpleasant Feeling	18 (35.29%)	17 (38.63%)	01 (14.28%)	0.56
s) Feeling helpless	23 (45.09%)	19 (43.18%)	04 (57.14%)	0.21

Statistical Observations

According to the statistical observations significant difference was observed among the responses of male and female participants concerning their awareness of PD. Moreover, the

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prevalence of disease occurrence was observed to be greater in male subjects in comparison to females which might support their feebler awareness of a particular disease. On the other hand, statistical observation ascribes that literate subjects were exhibiting greater awareness of PD with statistical results presenting significant differences ($P < 0.05$) among the responses of literate and illiterate individuals. In contrast, no significant difference ($P > 0.05$) was noticed among the responses of patients below and above 50 years suggesting no relationship of aging with the provoked occurrence of PD. The results of statistical interpretations are mentioned below in Table 5 and Figure 1.

Table 5: Statistical observations indicating the relationship of three different variables i.e. gender, education, and age with PD

Variable	Sample size	Mean ($\pm$ S.D)	T-value	P-value
Gender				
Males	44	4.62 ± 0.012	1.0687	0.00017
Females	07	2.18 ± 0.034		
Education				
Literate	32	3.198 ± 1.4107	4.1492	0.0001
Illiterate	19	3.1102 ± 0.3987		
Age				
Above 50 years	30	3.1093 ± 0.2607	3.8105	0.7926
Below 50 years	21	3.4487 ± 0.1986		

The analysis of the statistical correlation of motor symptoms with PD indicated a strong association of the described motor symptoms with PD as indicated by OR >1 along with a 95 % confidence interval (CI) of odd ratio. However, gender based relationship between these factors with PD presented no remarkable results signifying no association of gender with the defined motor symptoms. In contrast, the analysis of the statistical correlation of non-motor symptoms with PD indicated the strong correlation of all the described nonmotor symptoms with PD except loss of Interest, less expressive face, frightened feeling, and satisfactory life status suggesting no positive involvement of these non-motor symptoms with PD. However, a gender-based association of the non-motor symptoms with PD indicated a significant association of gender with all the respective symptoms except feeling blue or sad and troubles arising from the chair. The results of the statistical analysis are mentioned below in Table 6. Further statistical analysis of the relationship between different risk factors with PD occurrence indicated a significant correlation of only tobacco use with PD. Different motor and non-motor symptoms related to PD have been described in Figure 2.

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Table 6: Statistical analysis indicating the appearance of Motor and Non-Motor symptoms in male and female patients

Symptoms	All Patients	Male (n=44)	Female (n=7)	OR	95% CI	P values
Motor Symptoms						
Resting Shaking (tremor)	49 (96.07%)	42 (95.45%)	07 (100%)	1.63	0.96-2.80	0.56
Posture Instability	30 (58.82%)	24 (54.54%)	06 (85.71%)	1.11	0.19-1.56	0.12
Slow Walking	45 (88.23%)	39 (88.63%)	06 (85.71%)	1.98	0.112-3.12	0.82
Muscle Stiffness	35 (68.62%)	30 (68.18%)	05 (71.42%)	1.24	0.94-3.19	0.86
Non-Motor Symptoms						
Feeling Blue or Sad	26 (50.98%)	20 (45.45%)	06 (85.71%)	1.267	0.14-2.22	0.04*
Loss of Interest	40 (78.43%)	33 (75%)	07 (100%)	0.102	1.06-3.65	0.13
Sleep problem	31 (60.78%)	26 (59.09%)	05 (71.42%)	1.996	0.19-2.10	0.53
Memory problem	37 (72.54%)	31 (70.45%)	06 (85.71%)	1.4209	1.11-2.01	0.40
Difficulty in buttoning the button	34 (66.66%)	29 (65.90%)	05 (71.42%)	1.0107	2.22-3.76	0.77
Smaller handwriting	41 (80.39%)	36 (81.81%)	05 (71.42%)	0.1734	0.91-2.29	0.09
Troubles arising from the chair	35 (68.62%)	28 (63.63%)	07 (100%)	0.2022	1.45-3.82	0.05*
Softer Voice	37 (72.54%)	31 (70.45%)	06 (85.71%)	1.1130	0.14-2.71	0.40
Poor Balance	30 (58.82%)	25 (56.81%)	05 (71.42%)	1.5552	2.93-3.18	0.46
Less Expressive Face	33 (64.70%)	31 (70.45%)	05 (71.42%)	0.9103	0.54-2.15	0.68
Hearing/Seeing things	20 (39.21%)	18 (40.90%)	02 (28.57%)	1.5946	1.20-2.61	0.53
Anxiety illness	36 (70.58%)	32 (72.72%)	04 (57.14%)	1.3320	0.01-2.39	0.40
Weakness/dizziness	37 (72.54%)	32 (72.72%)	05 (71.42%)	1.7819	1.82-3.71	0.94
Hopelessness	18 (35.29%)	15 (34.09%)	03 (42.85%)	1.4187	2.66-3.19	0.65
Frighten feeling	26 (50.98%)	21 (47.72%)	05 (71.42%)	0.5410	0.39-1.91	0.24
Satisfactory Life status	33 (64.70%)	28 (63.63%)	05 (71.42%)	0.6654	1.56-2.81	0.65
Lack of Happiness in Life	23 (45.09%)	20 (45.45%)	03 (42.85%)	1.1176	2.09-3.61	0.89

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Unpleasant Feeling	18 (35.29%)	17 (38.63%)	01 (14.28%)	1.2309	0.57-1.69	0.56
Feeling helpless	23 (45.09%)	19 (43.18%)	04 (57.14%)	1.8909	1.78-2.06	0.21

Discussion

Parkinson's disease which results from the deficiency or abnormal functioning of dopamine-producing neurons in the extrapyramidal system is the second most pronounced neurological ailment after Alzheimer's disease. The neurological disorder may develop from the loss of dopamine-producing neurons in the extrapyramidal system [3, 17]. The substantia nigra pars compacta portion of the midbrain is comprised of several dopaminergic neurons, among which the lack of dopamine in the striatum may lead to PD [5, 7]. The four fundamental cardinal motor symptoms of PD include trembling of the arms and legs, slow movement, muscular rigidity, and instability of posture. PD is a slowly progressive disorder primarily affecting elderly people [17, 19]. The most prevalent non-motor symptoms (NMS), occurring during the course of the illness include REM sleep disruption, depression, and olfactory dysfunctions, occurring mostly in the early stages of the disease even before diagnosis. Certain symptoms of PD are common and may contribute to impairment and lowered quality of life [19-20]. In the Asian population, the higher prevalence of PD in male participants compared to female patients has been reported previously [22]. In contrast, an equal prevalence of PD in male and female subjects has been demonstrated in European countries [23]. Similarly, the findings of a higher prevalence of PD onset at later age are inconsistent with the previously reported study [15,16,23] According to the previous findings, comparative analysis of numerous populations indicated late-onset (88.2%) PD more frequently observed than young-onset (11.7%), with the mean age of about 60 years most frequently linked to PD disorder with the age of onset of current disorder being reported as 55 years [15,16,27]. Several reported studies described the presence of tremors in the early stages of Parkinson's disease with a progressive reduction in tremors occurrence as the conditions get worse [24]. Another important motor symptom of PD is the slowness of movement [25].

Micrographia is a Condition most commonly associated with PD and manifested as a small-print handwriting style [26]. In comparison to our results, other researchers have demonstrated comparatively lower memory-related outcomes [27-28]. Other reported studies suggested a comparatively lower occurrence of feeling faint, weak, or dizzy [8, 28]. Our findings of sleep disturbances correspond well with the findings of related studies, such as the Norwegian population study, that indicated experience of sleep disorders in approximately 60% of total cases [29-30]. The findings of a greater prevalence of feeling helplessness and hopelessness were also consistent with the previous study [31].

Conclusion

PD is a neurological disorder identified by patients feeling weak, dizzy, and unable to walk properly due to tremors, muscle stiffness, and rigidity. NMS is highly prevalent in patients

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with PD in the district of Abbottabad, KPK, Pakistan. Certain NMS are observed to be more frequent in female patients than male individuals. A thorough study is required to determine its underlying causes and any possible sex-based relation of PD NMS. Current study results and findings might be helpful in sorting out possible patient-related issues with successively improved patient care. The current study suggests the urgent need for awareness provision to the population of district Abbottabad, KPK, Pakistan regarding the occurrence, propagation, and possible outcomes of PD. In this regard, the pivotal role of public societies, governmental units particularly the scientific community, might be successfully upgraded.

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