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# INCIDENCE OF PSP IN PREVIOUSLY DIAGNOSED PARKINSON DISEASE PATIENTS

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**Abstract**

***Objective:*** *To observe the incidence of PSP in previously diagnosed Parkinson Disease Patients*

***Study Design:*** *A Descriptive Case Series*

***Study Duration:*** *06 months*

***Study Place:*** *Tertiary Care Hospital, Lahore*

***Methods:*** *A sample size of 110 was calculated using WHO calculator. Demographic data was taken. Patients were enrolled as per inclusion criteria. Detailed general physical and systemic examination was done. Patients were looked for the signs of the PSP and also detailed history about medication used and previous comorbids was also taken. The NINDS-SPSP was applied to diagnose PSP> All of these patients were those who had been previously diagnosed with Parkinson Disease. Data was analysed in SPPS version 23.*

***Results:*** *Total 110 patients were enrolled in our studies, among them 81 were males and 29 were females. The average onset of symptoms was 72±3 years. The most common symptom in our study was rigidity of trunk and knee muscles (94.5%), frontal cognitive defect which was evident in 93.6%, and then followed by downward gaze impairment (88.1%). Other symptoms include neck dystonia, convergence defects, apathy, disinhibition, frequent falls and difficulty falling asleep. Males were effected more in our study, with males effected thrice more than females.*

***Conclusion:*** *PSP is a rare disease and it relies on clinical diagnosis. The chances of a patient being diagnosed with Parkinson Disease is quite high, however detailed history and thorough examination is what required diagnosing patient with PSP.*

## INTRODUCTION

Progressive supranuclear palsy (PSP) is an uncommon neurological disorder that affects movement, gait, balance, speech, swallowing, vision, eye movements, mood, behavior, and cognition. It is an uncommon

neurological disorder, Progressive supranuclear palsy (PSP) is a form of atypical parkinsonian syndrome, also known as a Parkinson-plus disorder.[1] It was described as a constellation including supranuclear gaze palsy, progressive axial rigidity, pseudobulbar palsy, and mild dementia.[2] The disease was described in 1964 by Steele, Richardson, and Olszewski and in 1972, Steele predicted clinical variants of the syndrome were likely to occur as the disease affected different brainstem nuclei at different times and to different degrees.[3,4]

The cause of progressive supranuclear palsy is unknown. Advanced age and environmental factors such as exposure to toxins are theorized causes. The tau protein aggregates may be due to an unconventional infectious agent, random genetic mutations, or some unknown chemical in the food, air, or water which slowly damages certain vulnerable areas of the brain. Taupathy is a recognized cause of the neuro-degeneration in the PSP, and mutations in the gene encoding the microtubule-associated protein tau are associated with frontotemporal dementia and parkinsonism and parkinsonism plus syndrome linked to chromosome 17.[5,6]

The estimated annual prevalence of 5–7 per 100,000 persons and annual incidence density rate between 0.9 and 2.6 per 100,000 persons, which both increase with age.[7,8]

In contrast, Parkinson disease is a neurodegenerative disorder that mostly presents in later life with generalized slowing of movements (bradykinesia) and at least one other symptom of resting tremor or rigidity. Other associated features are a loss of smell, sleep dysfunction, mood disorders, excess salivation, constipation, and excessive periodic limb movements in sleep (REM behavior disorder). The mean age of presentation is 60 years and the first and most common symptom is resting tremor.[9]

In our study, we will observe the incidence of new onset Parkinson plus syndrome (PSP) in patients who have been previously diagnosed with Parkinson disease. We will observe the signs and symptoms of the patients which will lead us to diagnose PSP in these patients.

**Methodology:**

A total of 110 patients were included in our study. The study was conducted in Teritary Care Hospital Lahore from ____to____, after approval from institutional review board. A sample size of 110 was calculated by using WHO sample size calculator, and keeping confidence level 95% and margin of error 7.5%, population proportion was 50%. A descriptive case series was done which spanned for 06 months. Detailed demographic data including age, gender, occupation, education, and place of resident was noted. Patients were asked about their previous co-morbid, duration and medication of their co-morbid. All the participants were also asked about Parkinson symptoms and since when they had been labelled with Parkinsonism and whether they had been taking any treatment or not, and if treatment had proved beneficial or not. All the patients had been examined thoroughly for the sign and symptoms of progressive supranuclear palsy (PSP). The NINDS-SPSP criterion was applied, which includes 04 clinical aspects to diagnose a case of PSP.[10] Patients had also been investigated for all the previous and current radiological scans. Patients were explained about the objective of the study and an informed written consent was taken for inclusion in the study. The inclusion and exclusion criteria are as follow:

**Inclusion Criteria:**

1. Age above 40 years
2. Had been previously diagnosed or treated with Parkinson Disease
3. Willing to participate in study

**Exclusion Criteria:**

Age less than 40 years
Patients of CVA (Ischemic or Haemorrhagic stroke)
Unwilling for study
Diagnosis for Parkinson not cleared/known
Radiological evidence of SOL brain or malignancy

The data was analysed using SPSS version 23. Normally distributed variables were presented as mean and standard deviation. A p value of less than .05 was considered as statistical significant. Multiple Regression Model and Mann- Whitney equation was also used.

**Results:**

In our study, total 110 patients were included, among them 81(73.6%) were males and 29 (26.3%) were females. The most common symptoms reported in

our study was dystonia of neck muscles, frequent falls, impairment of downward gaze, loss of convergence, frontal cognitive deficit, behavioural problems like apathy and disinhibition and difficulty in falling or maintaining sleep. History of frequent falls was present in 94(85.4%) patients, among them males 61 (64.8%) were and females were 33 (35.1%).

Torticollitis i.e. dystonia of neck was present in 69 (62.7%) patients, and it was present in 42 (60.8%) males and 27 (39.1%) female patients. Rigidity of trunk and knee muscles was evident in 104 (94.5%) persons, with male to female ratio was 76:28 (73%, 26.9%)

The most frequent ocular symptom was impairment in downward gaze which was evident in 97 (88.1%) patients, and among them males were 69 (71.1%) and females were 28 (28.2%). Convergence defect was also seen in our study, with 53 (48.1%) subjects exhibiting loss of convergence, with male to female ratio being 32:21 (60.3%, 39.6%)

Apathy was exhibited by 91 (82.7%) patients, disinhibition by 72 (65.4%) patients and frontal cognitive deficits were seen in 103 (93.6%) patients. Among the 103 (93.6%) patients who exhibited cognitive defects, 79 (76.6%) were males and 24 (23.3%) were females.

The difficulty in falling asleep was found in 49 (44.5%) individuals only.

In our study, the most common symptom was rigidity of trunk and knee muscles was evident in 94.5%, followed by frontal cognitive defect (93.6%) and followed by impairment in downward gaze which was present in 88.1% people. Males were most effected in our study, and the average onset of symptom was at 72±3 years of age. The males were effected thrice more commonly than females.

| Symptoms | Gender | |
|---|---|---|
| | Male | Female |
| 1. Rigidity of trunk and knee muscles (94.5%) | 76 | 28 |
| 2. Frontal cognitive defect (93.6%) | 79 | 24 |
| 3. Downward gaze defect (88.1%) | 69 | 28 |
| 4. Torticollitis (62.7%) | 42 | 27 |
| 5. Convergence defect (48.1%) | 32 | 21 |
| 6. Disinhibition (65.4%) | 41 | 31 |
| 7. Apathy (82.7%) | 74 | 17 |
| 8. Insomnia (44.5%) | 29 | 20 |
| 9. Frequent falls (85.4%) | 61 | 33 |

**Table 1.1 (Symptoms observed in diagnosing PSP)**

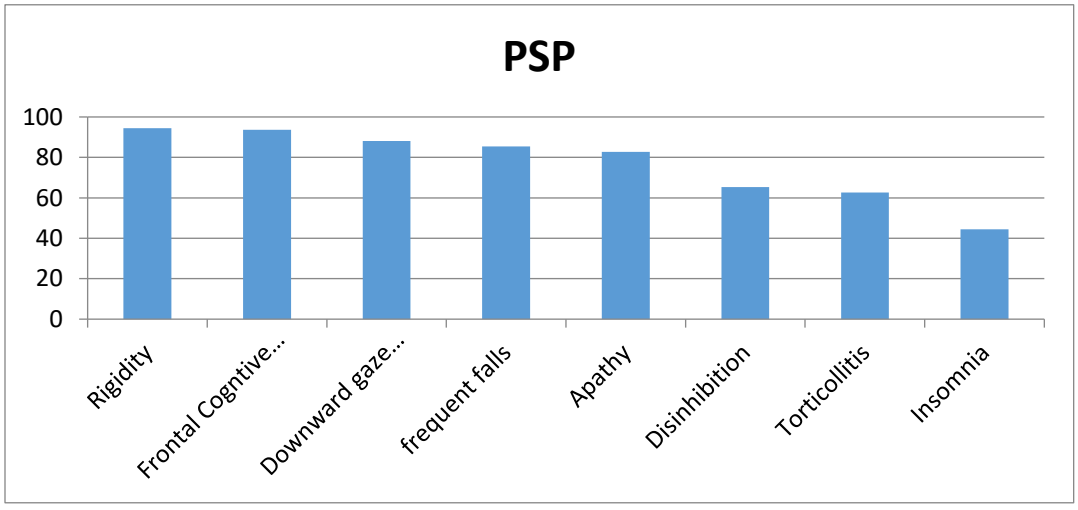


**Figure 1.1 (Symptom complex of PSP)**

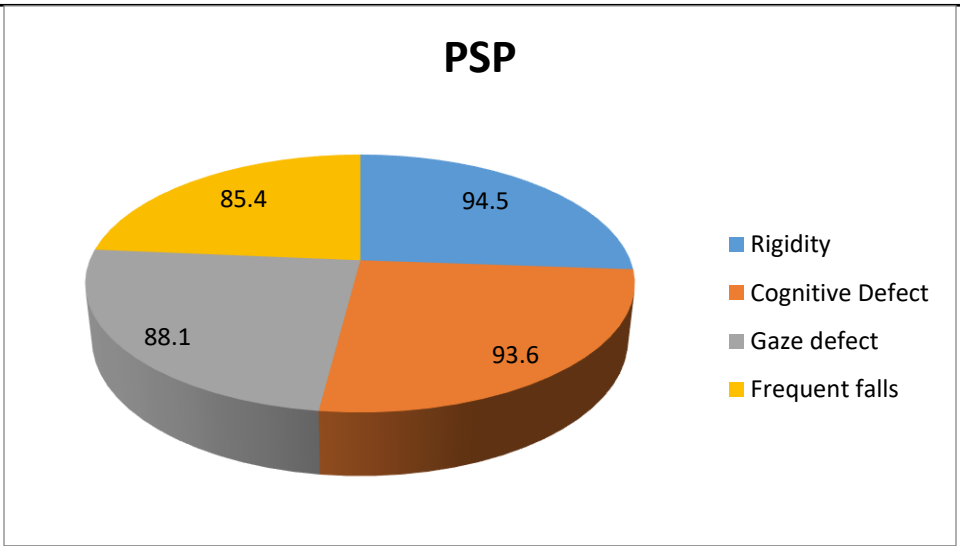


**Figure 1.2 (Pie Chart demonstrating most common symptoms of PSP)**

**Discussion:**

The condition was originally referenced in 1964 had a constellation of symptoms including supranuclear gaze palsy, progressive axial rigidity, pseudobulbar palsy, and mild dementia. The mean age of onset for progressive supranuclear palsy is approximately 65 years. The original report noted a strong male predominance of approximately 8 to 1.[11] The defining histopathologic feature of progressive supranuclear palsy is an intracerebral aggregation of the microtubule-associated protein tau with preferential involvement of the subthalamic nucleus, pallidum, striatum, red nucleus, substantia nigra, pontine tegmentum, oculomotor nucleus, medulla, and dentate nucleus.[12] In progressive supranuclear palsy and other tauopathies, the tau protein is hyperphosphorylated, which causes it to lose its affinity for microtubules and become resistant to proteolysis. This results in the accumulation of tau and the formation of neurofibrillary tangles.[13]

Progressive supranuclear palsy is an akinetic-rigid form of parkinsonism. Early in the course of the disease, motor abnormalities are typically axial and not appendicular. Gait difficulty and falls are the most common initial manifestation. Although supranuclear ophthalmoplegia is the hallmark of progressive supranuclear palsy, some patients only manifest this late in the progression of the disease. Slowed vertical saccades may be the only eye movement manifestation early on.[14]

The features of progressive supranuclear palsy includes impairment of downward gaze, impairment of vertical saccades, rigidity of axial muscles, dystonia of neck, frontal lobe dysfunction, impairment of memory and sleep disturbance.[15]

Lyon et ell did a meta-analysis which included 32 studies, in which 20 were prevalence studies and 12 were of incidence. Reported estimates of prevalence for PSP ranged from 1.00 (0.9–1.1) to 18 (8–28) per 100,000 and incidence rates for PSP ranged from 0.16 (0.07–0.39) to 2.6 per 100,000 person-years.[16]

Bower et ell did a study and found that the average annual incidence rate (new cases per 100,000 person-years) for ages 50 to 99 years was 5.3 for PSP and 3.0 for MSA. The incidence of PSP increased steeply with age from 1.7 at 50 to 59 years to 14.7 at 80 to 99 years, and was consistently higher in men. Median survival time from symptom onset was 5.3 years for PSP and 8.5 years for MSA.[17]

Progressive supranuclear palsy (PSP) represent challenging neurodegenerative disorders for clinicians and nonclinical scientists alike. Behavioral and cognitive changes are almost universal in PSP, with a wide range of reported deficits. Apathy is very common, often paradoxically accompanied by impulsivity.[18]

In our study, we included 110 individuals, who had shown signs and symptoms of progressive supranuclear palsy. PSP is rare entity and poses diagnostic challenges, however the most common symptoms encountered in our study was rigidity of

trunk and knee muscles, followed by frontal cognitive defect and downward gaze defects, as evident in study by Burell Jr et ell. In our study we also found patients with history of multiple falls off and on. Other symptoms which were also present in our study were loss of convergence defect, disinhintion, apathy and neck dystonias. The average age of symptom onset was 72 years in accordance with the study by Bower et ell.

**Limitations:**
This study is single center study with small population size and short span of study, hence its results cannot be generalized into a whole population. To get more results, a multi-center study should be done, with large population size and more duration of study.

**Conflict of study:** NIL

**Funding:** NIL

**Conclusion:**
Progressive Supra Nuclear Palsy is rare neurodegenerative disease, which mimcs Parkinson disease in its own set. However, Disease progression in progressive supranuclear palsy usually occurs fairly rapidly and relentlessly and patient detoriates rapidly. The disease is characterized by few prominent symptoms which help in distinguishing it from Parkinson disease, which include downward gaze impairment, apathy, truncal rigidity and frequent falls. It pathology is characterized by widespread neurodegeneration associated with tau protein deposition in subcortical regions. Hence, to diagnose a case of PSP, a high suspicion is required and keen observation of symptoms is required.

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