

Pattern of hospital admission and outcome in Parkinson's disease: A study from Punjab, India

¹Birinder Singh Paul MD DM, ²Gunchan Paul MD IDCCM, ¹Gagandeep Singh MD DM, ³Sandeep Kaushal MD, Verma U MBBS

¹Department of Neurology, ²Department of Critical Care, ³Department of Pharmacology, Dayanand Medical College & Hospital, Ludhiana

Abstract

Background: The hospitalization rates of patients with Parkinson's disease (PD) are 1.45 times higher than for age matched controls. We studied the causes for admission, hospital course and outcomes in PD population so that preventive measures could be developed. **Methods:** We prospectively studied patients with the diagnosis of PD admitted to a tertiary care hospital in Ludhiana, India from January, 2012 to December, 2014. Etiology for hospitalization was determined and the patients were divided into two groups, admission due to causes related to PD or not associated with PD. The PD related admissions were further categorized into Group I: directly disease related causes and Group II: indirectly disease related causes. The primary outcome was mortality. The secondary outcome measures were duration of hospitalization, requirement for ICU, need for mechanical ventilation and complications. **Results:** There were 146 patients of PD out of 25,326 hospital admissions. Forty two patients (28.7%) had direct cause, 73(50%) had indirect cause and 31(21.2%) were non-PD related admissions. The mean age was 68.5±9.9 years, 97males (66.7%). There were 16(10.9%) deaths. The commonest cause of admission was infections and encephalopathy. The indirect PD related admission had significantly higher age ($p=0.0014$), increased risk of ICU admission ($p=0.011$), need for mechanical ventilation ($p < 0.005$) and longer duration of hospital stay ($p=0.0001$) as compared to group I. Also there was a six fold increased risk of death in this group ($p 0.034$).

Conclusion: As disease progresses, the indirect reasons for admission becomes more troublesome than the initial motor complaints.

Key words: Parkinson's disease, hospital admission, mortality

INTRODUCTION

Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder with life time risk of 2% in men and 1.3% in women.¹ Although slowly progressive, this disorder has a significant impact on the quality of life due to its motor disability and non-motor manifestations.²⁻⁴ PD is commonly managed in the outpatient by physicians but in due course of time, wide range of complications become associated with the disease and may result in emergency hospitalization.^{5,6} These complications probably reflect a combination of disease progression, non-motor symptoms as well as medication induced complications. The hospitalization rates of patients with PD are 1.45 times higher than for age matched controls.⁷ The cause for hospital admission may be directly related to the disease progression (dyskinesia or motor fluctuations)

or indirectly related to the degenerative process (falls, infections) or may not be related to disease at all. By pre-emptive evaluation of the cause and effect relationship it might be possible to reduce the number of admissions which are related to the disease. This will result in reduction the morbidity and mortality related to PD. Also, it will help to reduce the financial burden on the patients. Thus, the aim of this study was to analyze the causes for hospital admission and their outcomes in PD population and determine the possible preventive measures.

METHODS

We prospectively studied all adult patients with the known diagnosis of PD admitted either to the emergency room, ward or intensive care unit of a tertiary care teaching hospital from January,

2012 to December, 2014. The diagnosis of PD were according to the United Kingdom Parkinson Disease Society Brain Bank criteria (UKBB) criteria. The protocol of this study was approved by the institutional ethics committee.

Clinical characteristics, investigational data, treatment and outcome of the patients were recorded. The demographic and clinical parameters that were entered on a pre-designed Performa included age, gender, age of onset, duration of disease, modified Hoehn-Yahr (H&Y) staging (prior to admission), associated co-morbid conditions, treatment history, non compliance (arbitrarily regarded as missing two or more doses in a day, two or more times per week), number of admission in past one year, reason for admission and complications during the hospital stay (bed sore, hospital acquired infections, deep vein thrombosis, death). In patients with recurrent admissions during the study period, each admission was recorded as a separate event. Patients with insufficient data regarding diagnosis, incorrect diagnosis or secondary parkinsonism were excluded.

Based on the aetiology for hospital admission, patients were divided in two groups, admission

due to causes related to PD or not associated with PD (Figure 1). The PD related admissions were further categorized into Group I: *directly disease related* causes including motor complications, dose adjustments, side effects of anti-parkinsonian medications and Group II- *indirectly disease related causes* including falls, trauma, delirium (detected using the confusion assessment method-CAM score), aspiration pneumonia, urinary tract infection or retention, severe gastro-intestinal disturbance (constipation or diarrhoea), electrolyte disturbances (hyponatremia-<130meq/L, hypernatremia->145meq/L, hypomagnesemia-<1.5meq/L, hypocalcemia-<8.5meq/L). *Non-PD related situations* included myocardial infarction, congestive cardiac failure, cerebrovascular disease or renal failure etc.

The primary outcome was mortality at hospital discharge. The secondary outcome measures were duration of hospitalization (days), requirement for ICU (as per the standard protocol of the hospital), need for mechanical ventilation and complications during hospital stay. Factors potentially affecting hospital admission and course were analyzed by comparing the two groups. All values were expressed as mean (\pm SD) and percentages using

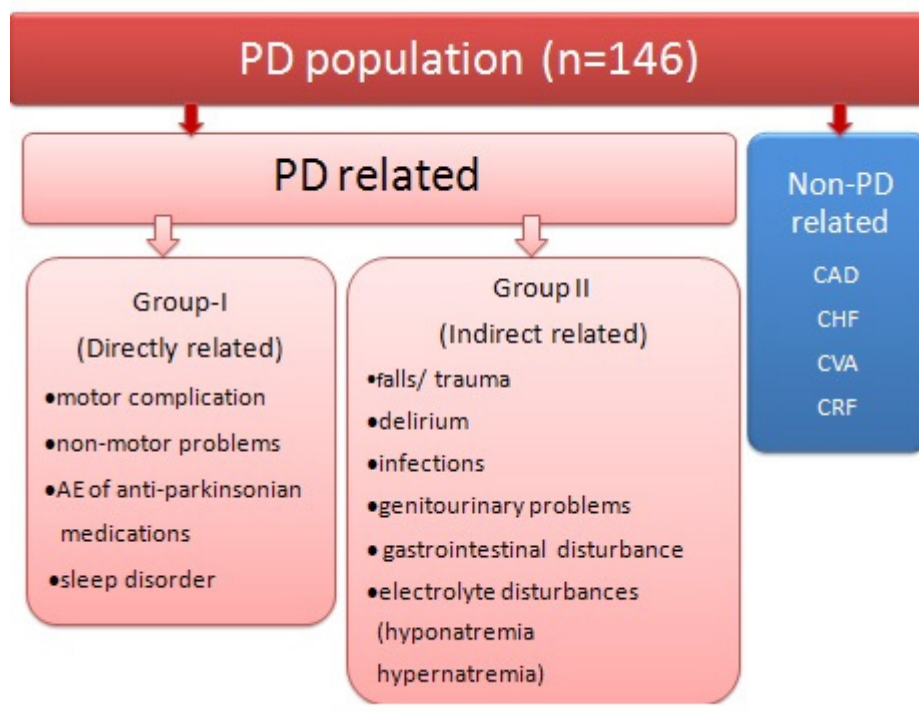


Figure 1. Division of the Parkinson’s disease population based on various causes of admission. (PD, Parkinson’s disease; CAD, coronary artery disease; CHG, congestive heart failure; CVA, cerebrovascular accident; CRF, chronic renal failure)

Table1: Demographic profile and details of hospitalization of all patients of Parkinson's disease admitted during the three year period

Clinical Parameters	N = 146
Mean Age (years)	68.52 ± 9.9
Male (%)	97 (66.4%)
Duration of disease (years)	3.87 ± 2.89
Hoehn and Yahr	2.79 ± 0.81
<3	61
>3	85
Co morbid conditions	59 (40.1%)
• DM alone	16
• HTN alone	20
• DM & HTN	13
• DM, HTN & CAD	9
• DM, HTN & CRF	1
Duration of Hospital stay (days)	7.64 ± 5.83
ICU admission (%)	42 (28.7%)
Complications	28 (19.1%)
• Bed sore	4
• HAI	7
• DVT	1
• Death	16
Previous admission	16

DM, diabetes mellitus; HTN, hypertension; CAD, coronary artery disease; CRF, chronic renal failure; HAI, hospital acquired infection; DVT, deep vein thrombosis

SPSS 16.0. Paired t-test was used for categorical variables and chi square was used for continuous variables. The p-value < 0.05 was considered to be significant.

RESULTS

During the three years study period there were total 25,326 admissions in the hospital. Of these 146 (0.06%) patients had the diagnosis of PD that fulfilled our inclusion criteria. The age of the cohort ranged from 42-92 years, with a mean of 68.5 ± 9.9 years. There were 97 males (66.7%), and 49 females (33.3%). Table 1 shows the demographic profile and details of hospitalization of all the patients of PD.

With respect to aetiology of admission, 42 patients (35.6%) had direct cause, 73 (50%) had indirect disease related cause and 31 (21.2%) had non-PD related admission. However, there was an overlap of 9 patients in the indirect group which had associated motor complications. Hence, these were included in both the groups for analysis, resulting in the PD related admissions to be 51 in Group I and 73 in Group II. Table 2 depicts the

cause of hospital admission of all PD patients.

Sixteen (10.3%) patients had history of previous admission, further categorization of hospitalization either due to direct, indirect and non-PD related were three, eleven and two respectively. Ninety eight (67.1%) patients were compliant to treatment. 59 patients (40.4%) had associated co-morbid conditions and 57 (97%) were on regular treatment for these medical disorders.

The mean duration of hospitalization was 7.64 ± 5.83 days (range, 2-17 days). Duration of hospitalization was significantly shorter for patients in Group I, 6.38 ± 5.53 days as compared to 9.2 ± 6.80 days in Group II. During the hospital course, 42 (28.7%) patients required ICU admission, 20 (13.7%) required mechanical ventilation out of which 11 patients were admitted with indirect cause and 7 admission were non-PD related, while one had direct cause and the other had both direct and indirect reason.

There were 16 (10.9%) deaths in our series. Outcome was worst in the indirect group with 56.2% mortality (9 patients), followed by 31.2%

Table 2: Etiology of hospital admission among all Parkinson's disease patients

PD –related	n (%)
• Direct disease related	51
a. Motor symptoms & levodopa related motor complication	38
b. Neuropsychiatry symptoms	4
c. Motor symptoms & associated indirect cause	9
• Indirect disease related	73
a. Infections	30 (20.5)
- Pneumonia	14
- UTI	11
- Undiagnosed source	5
b. Encephalopathy	27 (18.4)
- Electrolyte disturbances	17
- Delirium unexplained	10
c. Trauma	13 (8.9)
- Fractures	10
- SDH	3
d. Gastrointestinal	3 (2)
- Paralytic ileus	2
- Perforation	1
Non PD related	31
• CCF	10
• CRF	8
• ACS	8
• CVA	5

PD, Parkinson's disease; UTI, urinary tract infection; SDH, subdural hematoma; CCF, congestive cardiac failure; CRF, chronic renal failure; ACS, acute coronary syndrome, CVA, cerebrovascular accident

mortality (5 patients) in the non-PD related group. Only one patient belonged to group I (6.3%) while one patient (6.3%) had both directly and indirectly PD related cause for hospitalization. This study revealed that there was a significant difference in mortality between the two groups ($p=0.034$).

In patients whom the cause of hospital admission was indirectly related to PD had significantly higher age ($p=0.0014$), increased risk of ICU admission ($p=0.011$), longer duration of hospital stay (9.22 ± 6.80 ; $p=0.0001$) and need for mechanical ventilation ($p<0.005$) as compared to group I (Table 3). There was also a trend of poor outcome in these patients in relation to repeated admissions and complications, although the difference was not statistically significant. However, there was no correlation with respect to gender, duration of disease and H & Y stage with either cause of hospital admission or outcome.

Thus, our study showed that poor outcome of hospital admission as predicted by duration of hospitalization, need for ICU admission and mortality was significantly associated with indirect disease related causes for admission in PD patients.

DISCUSSION

In this study we aimed to identify the causes for hospitalization and outcome of admission in patients with PD. The first step was to categorize the patients according to the causes for hospital admission as related or not related to the PD. Then we separated the PD related patients as either directly or indirectly related to Parkinson disease itself. This was done in order to find out the true impact of the disease on hospital admission and outcome. PD patients when admitted with causes such as strokes, coronary artery disease or renal failure, that are likely not to be related to PD and dependent on the associated co morbid conditions, were excluded for analysis (non PD related group).

In our study the commonest reason for admission to hospital was the indirect disease related cause, which constituted about 50% of the admissions (Figure 2). Infectious diseases (40.5%) particularly pneumonia and urinary tract infection (UTI) were the major indirect reasons for admission. This is in accordance with the previous studies that report infections followed

Table 3: The comparison of outcome parameters between the direct (Group I) and indirect (Group II) group of Parkinson's disease patients

Characteristic	Directly related to PD (Group I) n-51	Indirectly related to PD (Group II) n-73	p value
Mean Age (years, range)	64.56 ± 9.14 (4-85)	70.93 ± 9.32 (49-90)	0.0014
Gender (Male)	34 (65.4)	49 (67.1)	0.14
Duration of disease (years)	3.77 ± 2.55	4.52 ± 3.23	0.014
H & Y stage	2.71 ± 0.82	2.97 ± 0.78	0.078
Co morbid conditions	21 (40.4)	35 (47.9)	0.67
Duration of hospital stay (days)	6.38 ± 5.53	9.2 ± 6.80	0.0001
ICU admission	3 (5.7)	25 (34.2)	0.011
Mechanical ventilation	1 (1.9)	12 (16.4)	<0.005
Complications	8 (15.4)	20 (27.3)	0.11
Death	1 (1.9)	9 (12.5)	0.034
Previous admission	3 (5.7)	11 (15)	0.104

*Values given in parenthesis are the percentages p value < 0.05 is considered significant
PD, Parkinson's disease; H&Y, Hoehn & Yahr

by trauma as the commonest reasons for hospital admission⁷⁻¹¹, although the precise proportions differ, probably due to regional differences. Guneyzel *et al.* have reported infections (31.6%) as the commonest reason for hospitalization.¹² Similarly, Tan *et al.* reported pneumonia in 13% of 761 admitted PD patients.¹³ These infections

are indirectly related to PD because as the disease progresses dysphagia and autonomic dysfunction become fairly common, increasing the risk of aspiration and bladder dysfunction. In addition, there is marked reduction in mobility in these patients in the later stages of disease.

In our study, encephalopathy was the second

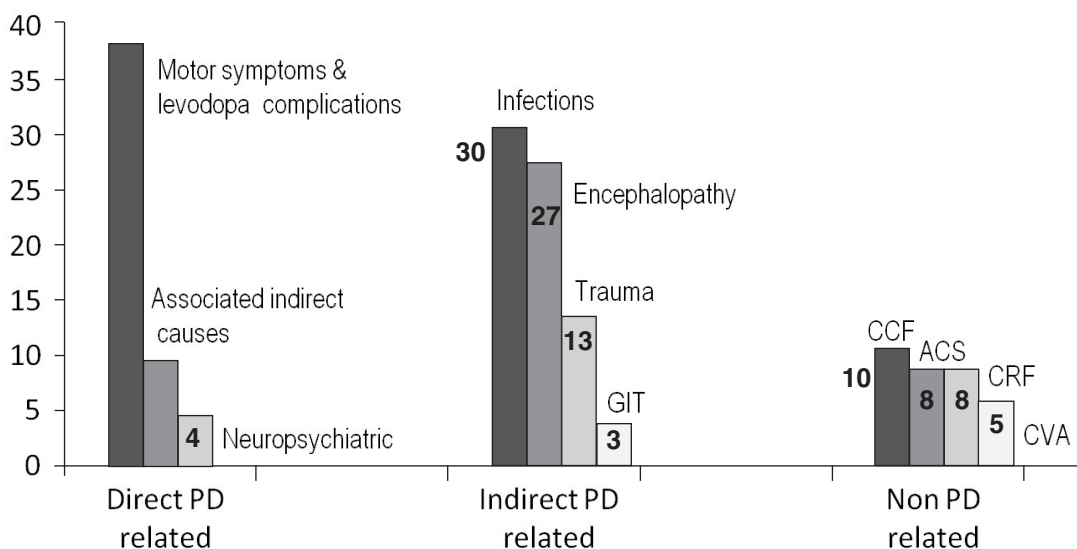


Figure 2. Bar Graph depicting the various causes of admission among Parkinson's disease patients. (PD, Parkinson's disease; CCF, congestive cardiac failure; ACS, acute coronary syndrome; CRF, chronic renal failure; CVA, cerebrovascular accident)

commonest cause for admission in about 18.4% patients. Electrolyte disturbances, especially hyponatremia was the commonest reason for the same, though Guneyssel *et al.* have reported a much lower incidence of electrolyte disturbances, only 6.5% as a cause of admission.¹² On analysis of the metabolic causes, we found that 40% of our patients with hyponatremia were receiving diuretics (chlorthiazide) for associated hypertension. Also, some PD patients have autonomic and gastrointestinal dysfunction combined with reduced intake of food. Though a direct cause and effect relation is difficult to establish but a combination of these factors could contribute to the high incidence of electrolyte disturbance in our series. Such factors are seldom brought into consideration but may contribute to the electrolyte imbalance in the already existing unstable scenario of PD sufferers. Hence, we recommend a cautious use of diuretics as anti-hypertensives in this subset of patients, along with frequent monitoring of electrolytes.

PD patients have progressive postural instability or freezing which leads to frequent falls resulting in trauma.¹⁴ In our study 8.9% patients had either severe head injury (subdural haemorrhage) or fractures. Previous studies have reported a similar incidence of 11% to 27.6% of emergency admissions among PD patients due to falls and fractures.^{15,16}

A community based epidemiological study by Das *et al.* from West Bengal found maximum mortality among PD patients in the age band of 70- 74 years with mean age 71.31 yr.¹⁷ Similarly in our study the mean age of the indirect group which had a higher mortality was 70.93 years.

In the neurodegenerative disorders such as PD, when age increases there is linear reduction of body reserves in these already vulnerable patients. Any new ailment leads to fast deterioration in the patient condition. This sets a vicious cycle of progressive downhill course, prolonging the hospital stay, risk of mechanical ventilation, hospital complications and increased mortality. In our study, the PD patients who were hospitalized with indirect cause had increased duration of hospital stay, need for ICU admission and increased mortality as compared to the direct disease related group. This shows that emergency admissions were more dependent on age and non-neurological reasons rather than only being related to the progress of the primary disease. A community based study from east India found 13 PD related deaths in a cohort of 100,000 population, with an average annual mortality

rate of 2.28 (1.21-3.80).¹⁷ In our hospital based study there were 16 deaths over a period of three years with 9 deaths in the indirect group, which was statistically significant as compared to the direct group ($p=0.034$). The percentage of patients who had associated co-morbid diseases was comparable in both the groups which could not be the cause of this disparity. This observation showed that on comparison of the two groups, there was a six fold increased risk of death in PD patients who were admitted to the hospital with indirect reason related to PD. Vincent *et al.* have also reported increased mortality in PD patients as compared to control with a proportional mortality rate of 2.46 (95% CI 2.42-2.49, $p<0.0001$) though they have not analyzed the cause of death based on reason of admissions.¹⁸ While Goldberg *et al.* also report that PD patients when admitted have 2.5 times more risk of dying.¹⁹

We conclude that one should recognize the importance PD as a possible cause of co-morbidity. As the disease progresses, the indirect reasons for admission become more troublesome than the initial motor complaints requiring frequent hospitalization. As life expectancy of PD patients is increasing so are the complications as well as the hospital admissions. The preventive strategies to reduce in the number of admissions are: 1)Recognizing early symptoms and signs of infection by vigilance and education of the care givers;2) Extra attention to prevent falls and strengthening of safety features such as encouraging the use of hand held rails; 3)Cautious use of non-dopaminergic drugs as their side effects can severely affect the already existing unstable scenario of PD sufferers eg diuretic as anti-hypertensive necessitates frequent monitoring of electrolytes.

There are limitations of our study, as some cases may have been missed as data collection was manual. There may be also be referral bias as ours is a tertiary care hospital where only complicated or unwell PD patients have been referred while others may have been managed in the periphery. These limitations could have led to under-estimation of the size of the problem.

DISCLOSURE

Source(s) of support: None

Conflict of interest: None

REFERENCES

1. MacDonald BK, Cockerell OC, Sander JW, Shorvon

- SD. The incidence and lifetime prevalence of neurological disorders in a prospective community based study in the UK. *Brain* 2000; 123:665-76.
2. Arasalingam A, Clarke CE. Reasons for Parkinson's disease admissions in a large inner city hospital. *Parkinsonism Relat Disord* 2014; 20:237e8.
 3. Chaudhuri KR, Healy DG, Schapira AH. Non-motor symptoms of Parkinson's disease: diagnosis and management. *Lancet Neurol* 2006; 5(3):235-45.
 4. Lim SY, Lang AE. The nonmotor symptoms of Parkinson's disease: An overview. *Mov Disord* 2010; 25(Suppl. 1):S123-30.
 5. Chou KL, Zamudio J, Schmidt P, *et al.* Hospitalization in Parkinson disease: A survey of National Parkinson Foundation Centers. *Parkinsonism Relat Disord* 2011;17:440-5.
 6. Hassan A, Wu SS, Schmidt P, *et al.* High rates and the risk factors for emergency room visits and hospitalization in Parkinson's disease. *Parkinsonism Relat Disord* 2013; 19:949-54.
 7. Chen RC, Chang SF, Su CL, *et al.* Prevalence, incidence and mortality of PD: a door-to-door survey in Ilan country, Taiwan. *Neurology* 2001;57:1679-1686.
 8. Klein C, Prokhorov T, Miniovitz A, Dobronevsky E, Rabey J. Admission of Parkinsonian patients to a neurological ward in a community hospital. *J Neural Transm* 2009;116:1509e12.
 9. Chapuis S, Ouchchane L, Metz O, Gerbaud L, Durif F. Impact of the motor complications of Parkinson's disease on the quality of life. *Mov Disord* 2005; 20:224-30.
 10. Guttman M, Slaughter PM, Theriault ME, Deboer DP, Naylor CD. Parkinsonism in Ontario: comorbidity associated with hospitalization in a large cohort. *Mov Disord* 2004; 19:49-53.
 11. Woodford H, Walker R. Emergency hospital admissions in idiopathic Parkinson's disease. *Mov Disord* 2005; 20:1104e8.
 12. Guneyssel O, Onultan O, Onur O. Parkinson's disease and the frequent reasons for emergency admission. *Neuropsychiatr Dis Treat* 2008; 4:711-14.
 13. Tan LCS, Tan AKY, Tjia HTL. The profile of hospitalized patients with Parkinson's disease. *Ann Acad Med Singapore* 1998; c27:808-12.
 14. Factor SA, Molho ES. Emergency department presentations of patients with Parkinson's disease. *Am J Emerg Med* 2000; 18:209-15.
 15. Temlett JA, Thompson PD. Reasons for admission to hospital for Parkinson's disease. *Intern Med J* 2006; 36:524-6.
 16. Vossius C, Nilsen OB, Larsen JP. Parkinson's disease and hospital admissions: frequencies, diagnoses and costs. *Acta Neurol Scand* 2010; 121:38-43.
 17. Das SK, Misra AK, Ray BK, *et al.* Epidemiology of Parkinson's disease in the city of Kolkata, India. A community-based study. *Neurology* 2010; 75:1362-9.
 18. Low V, Ben-Shlomo Y, Coward E, Fletcher S, Walker R, Clarke CE. Measuring the burden and mortality of hospitalisation in Parkinson's disease: A cross-sectional analysis of the English Hospital Episodes Statistics database 2009-2013. *Parkinsonism Relat Disord* 2015; 21: 449-54.
 19. Goldberg ID, Kurland LT. Mortality in 33 countries from disease of the nervous system. *World Neurol* 1962 Jun; 3:444-65.