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# Main reasons for hospital admission in patients with Parkinson's disease and their relationship with the days of hospitalization

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## Abstract

**Objective:** *It is necessary to study the main comorbidities of Parkinson's disease that causes this increase in hospitalization. The aim of the study was to compare the mean days of hospital stay of patients with Parkinson's disease plus a comorbidity against the mean days of hospital stay without that comorbidity and to report those which were statistically significant.* **Methods:** *Taking patients with PD from "1 de octubre" Hospital, an observational, retrospective, cross-sectional, and analytical study was carried out in which the relationship of days of hospitalization with and without comorbidities was evaluated, finding which would be the comorbidities that were they become a factor of protection or risk of prolonging the hospital stay of patients with Parkinson's disease (PD) and thus suggest the priority of treating these conditions.* **Results:** *Of the 37 patients, 14 different comorbidities were found, of which hypothyroidism ($\bar{x}$ = 2), acute myocardial infarction/dyslipidemia ($\bar{x}$ = 4), and traumatic brain injury ($\bar{x}$ = 4) present a decrease in the number of days hospitalized patients with respect to the mean of patients who do not have these comorbidities, in comparison, sacral ulcer ($\bar{x}$ = 32.5) and pneumonia ($\bar{x}$ = 31) show an increase in the days of hospitalization with respect to the mean.* **Conclusion:** *Fourteen comorbidities were found in PD. Patients with sacral ulcer and pneumonia are hospitalized for a longer time compared to the different comorbidities. It is recommended to pay special attention and care to prevent/treat these pathologies to reduce the number of days of hospitalization.*

***Keywords:*** *Parkinson's disease. Comorbidities. Hospitalization. Disorders. Clinical studies.*

## *Principales motivos de ingreso hospitalario en pacientes con enfermedad de Parkinson y su relación con los días de hospitalización*

## Resumen

**Objetivo:** *Es necesario estudiar las principales comorbilidades de la enfermedad de Parkinson que provocan este aumento de hospitalizaciones. Comparar el promedio de días de estancia hospitalaria de los pacientes con enfermedad de Parkinson más una comorbilidad contra el promedio de días de estancia hospitalaria sin esa comorbilidad e informar aquellos que fueron estadísticamente significativos.* **Metodología:** *Tomando pacientes con EP desde el Hospital "1 de*

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*octubre", se realizó un estudio observacional, retrospectivo, transversal y analítico en el que se evaluó la relación de los días de hospitalización con y sin comorbilidades, encontrando cuáles serían las comorbilidades que se convierten en un factor de protección o riesgo de prolongar la estancia hospitalaria de los pacientes con EP y así sugerir la prioridad del tratamiento de estas condiciones.* **Resultados:** *De los 37 pacientes se encontraron 14 comorbilidades diferentes, de las cuales Hipotiroidismo ($\bar{x}$ = 2), Infarto agudo de miocardio/dislipidemia ($\bar{x}$ = 4), TCE ($\bar{x}$ = 4), presentan una disminución en el número de días Pacientes hospitalizados con respecto a la media de pacientes que no presentan estas comorbilidades, en comparación, úlcera sacra ($\bar{x}$ = 32,5) y neumonía ($\bar{x}$ = 31) muestran un aumento de los días de hospitalización con respecto a la media.* **Conclusión:** *Se encontraron 14 comorbilidades en la enfermedad de Parkinson. Los pacientes con úlcera sacra y neumonía son hospitalizados por más tiempo en comparación con las diferentes comorbilidades. Se recomienda prestar especial atención y cuidado para prevenir/tratar estas patologías para reducir el número de días de hospitalización.*

***Palabras clave:*** *Enfermedad de Parkinson. Comorbilidades. Hospitalización. Trastornos. Estudios clínicos.*

## Introduction

Parkinson's disease (PD) is a complex neurodegenerative disease that manifests itself through a variety of motor (resting tremors, rigidity, bradykinesia, and postural instability) and non-motor symptoms[1]. Its incidence increases with age and due to this, manifestation of this condition among the population depends on this factor[2-5]. As far the non-motor manifestations during the course of PD, many patients experience neuropsychiatric disorders (depression, anxiety, sleep disturbances, psychosis, behavioral changes, etc.)[6-10].

For PD to exacerbate to a severe disease, the appearance of comorbidities presents a risk factor, where some of these include hypertension, diabetes mellitus, pneumonia, dementia, cancer, high blood pressure, sepsis, edema, and heart failure, among others[11,12]. Furthermore, up to 80% of PD patients had five or more comorbidities[13]. The importance of this lies not only in patient complications, but also in the concomitant therapy of these medical diseases, given that it can seriously influence the success of the overall treatment or the mortality rate due to the administration of medications that involve alterations of the dopaminergic system.

From an observational and perspective, the reports that have been prepared involve three main study subgroups, which are: medical comorbidity (regardless of the underlying disease), clinical symptoms that arise as a result of the autonomic denervation associated with the disease, and the side effects of PD[9-45] an interesting area of focus is the analysis of the relationship between these comorbidities and length of hospital stay in patients with PD, given that in case–control and retrospective studies it has been shown that the risk of PD exacerbation depends on some comorbidity[14]. The analysis of the relationship between PD patients and their length of hospital stay based on comorbidities is undoubtedly a key study to learn more about Parkinson's and patients' length of hospital stay.

## Methodology

### *Study subjects*

All patients (n = 57) were selected from the Mexico City database who presented PD plus comorbidity that forced them to be hospitalized during the year 2021 (January 1-December 31). An observational, retrospective, cross-sectional, and analytical study was carried out, which evaluated the days of hospitalization in the presence of comorbidities. The patients were divided into two groups, those with the comorbidity in question (e.g., With sepsis) and those without the comorbidity (e.g., Without sepsis). Each group was given the average days of hospitalization and its standard deviation. The number of individuals chosen for the final study included those with a complete clinical history, where a total of 37 subjects with PD had some type of comorbidity that led them to hospitalization. The exclusion criteria were patients who were initially hospitalized for PD and not for their comorbidity or who had an incomplete or confusing medical record (20 patients). The dependent variable was the days of hospitalization (discrete quantitative variable) that were found in the comorbidities of Parkinson's disease, this data were obtained through electronic records during January 2022. Days of hospitalization were defined as the 1st day in which the patient was admitted to internal medicine or another specialty until the last day, he was discharged. The objective of this article is to compare

the mean days of hospital stay of patients with Parkinson's disease plus a comorbidity (e.g., sepsis) against the mean days of hospital stay without that comorbidity (e.g., without sepsis) and to report those which were statistically significant. The distribution of the study patients is shown in table 1.

### *Statistical analysis*

To demonstrate normality in the data, the Kolmogorov–Smirnov test reinforced with Lilliefors was used, which yielded a p = 0.08. The Shapiro–Wilk hypothesis test was performed for homogeneity of variances, where p = 0.0006 was obtained, so it was decided to perform a non-parametric chi-square test to compare the average hospital stay for all comorbidities and the mean length of hospital stay for each PD comorbidity. Statistical analysis was obtained using the R statistical package and the IDE R studio.

## Results

The most of the patients with PD were older adults, as expected, given that it is a risk factor for this disease. There were no differences between men and women.

Of the 37 patients, 14 different comorbidities were found. Hypothyroidism, acute myocardial infarction (AMI)/dyslipidemia, and cranioencephalic trauma (CET) have a lower average number of hospitalization days with regards to the mean of patients who do not have these comorbidities, on the other hand, sacral ulcer and pneumonia have a higher average of hospitalization days with regards to the mean (Table 2).

## Discussion

In this study, 14 individual or combined comorbidity risk factors were identified in patients with PD, who belonged to the database of the Hospital 1 de octubre. These associated comorbidity factors may be of pathogenic importance in PD. In this analysis, we found important relationships based on the comorbidities associated with PD patients, where it was detected that those with factors such as sacral ulcer and pneumonia had a longer hospitalization mean than those who exhibited comorbidities such as Hypothyroidism, AMI/dyslipidemia, and CET whereby their hospitalization relationship was less prolonged. Therefore, the association relationship is due to a chain of pathological effects that are discussed below:

**Table 1.** Number of PD patients who belong to the Hospital 1 de octubre

| Variables | Frequency | Percentage |
|---|---|---|
| Sex | | |
| Males | 19 | 51.4 |
| Females | 18 | 48.6 |
| Age | | |
| ≤ 59 | 6 | 16.2 |
| ≥ 60 | 31 | 83.8 |

PD: Parkinson's disease.

### *Pneumonia as a factor associated with longer hospitalization days in Parkinson's disease patients*

Pneumonia is lung inflammation in which the air sacs are filled with infectious secretions and other fluids, making it difficult for oxygen to reach the blood; in PD patients, pneumonia is not only an associated and risk factor, but it is also one of the main associated comorbidities that exacerbate the patient's health, which coincides with our study[15,16]. It has been studied that aspiration pneumonia cases have a higher incidence in individuals with PD, representing up to a 70% death rate of these patients, especially due to aspiration pneumonia that leads to oropharyngeal dysphagia[17,18]. In addition, it is known that aspiration pneumonia has a multifactorial effect in PD in which old age, male gender, region of residence, DM, congestive heart failure, tuberculosis, atrial fibrillation, cerebrovascular disease, dementia, seizure disorders, and use of antidiabetic drugs are associated with an increased risk of pneumonia and as risk factors for hospitalization[5,9,18,19]. The foregoing is consistent with the data from our study in which various associated comorbidities are observed (Table 2), showing that pneumonia is a relevant comorbidity factor that prolongs the length of hospital stay of PD patients. In our study, the exhibited pneumonia was due to aspiration, since it is known that PD patients exhibit esophageal hypomotility.

The link between the various comorbidities, including pneumonia, with the risk of prolonged hospitalization is important to identify and personalize the patient's medical care, given that it has been observed that with treated dental cavities there is also a link of decreased risk of hospitalization due to pneumonia in PD patients, where this is a protective factor when it comes to implementing the treatment[18,19].

**Table 2.** Average of days of hospitalization of patients with different comorbidities and the Chi-square test of independence

| Comorbidity | Frequency | Hospital days W/C | Hospital days Wo/C | $\chi^2$ | p-value |
|---|---|---|---|---|---|
| | | $\bar{x}$ (SD) | $\bar{x}$ (SD) | | |
| Hypothyroidism | 2 | 2 (2) | 17 (19) | 11.8 | < 0.001 |
| AMI/dyslipidemia | 3 | 4 (4) | 17 (19) | 8.04 | < 0.001 |
| CET | 2 | 4 (0.7) | 17 (19) | 8.04 | < 0.001 |
| Sacral ulcer | 6 | 32.5 (27) | 13 (15) | 8.35 | 0.03 |
| Pneumonia | 8 | 31 (34) | 12 (9) | 8.39 | 0.03 |
| Epilepsy | 2 | 8 (5) | 17 (19) | 3.24 | 0.07 |
| CVE | 9 | 9 (8) | 18 (20) | 3 | 0.08 |
| Cancer | 1 | 23 (23) | 16 (19) | 1.25 | 0.20 |
| UTI | 12 | 20 (20) | 14 (18) | 1.05 | 0.30 |
| Dementia | 5 | 20 (16) | 15 (19) | 0.7 | 0.30 |
| Delirium | 11 | 19 (19) | 15 (19) | 0.47 | 0.49 |
| Sepsis | 3 | 15 (5) | 16 (19) | 0.03 | 0.80 |
| SAH/hypertensive urgency | 19 | 16 (23) | 16 (13) | 0 | 1 |
| T2DM/diabetic cetoacidosis/hyperosmolar non-ketotic hyperglycemia | 10 | 16 (25) | 16 (16) | 0 | 1 |

AMI: acute myocardial infarction; CET: cranioencephalic trauma; CVE: cardiovascular event; PD: Parkinson's disease; SAH: systemic arterial hypertension; SD: standard deviation; T2DM: type 2 diabetes mellitus; UTI: urinary tract infection; W/C: with comorbidity; Wo/C: without comorbidity.

It is important not to underestimate the fact that pneumonia in PD patients leads to other risk factors for longer hospitalization, such as chronic heart failure, kidney disease, and oral hygiene. Sepsis is an additional factor not only due to the presence of pneumonia but also as a comorbidity that can trigger its development[5,20], implying that the length of hospitalization increases as a result of the treatments and the patient's recovery time; therefore, early recognition and immediate handling of physical illnesses/comorbidities such as pneumonia in PD patients can help reduce the risk or decrease hospitalization and, therefore, the burden of the disease.

## *Sacral ulcer, an important comorbidity factor associated with the length of hospitalization days of Parkinson's disease patients*

Given the fact that some of the main PD symptoms involves the incidence of involuntary tremors of certain body parts, slow movement, and rigid and inflexible muscles, they worsen as the disease progresses, which plays a relevant and treatment role in cases where PD patients are hospitalized, since the immobility of their stages due to the disease or other comorbidities leads to the development of sacral ulcers or pressure ulcers that, together with urinary/fecal incontinence, increase the risk of these types of ulcers[21,22]. In addition, the appearance of ulcers is not exclusively or directly associated with the immobility of PD patients during their hospitalization, instead the contracture or stiffness given their resting position, or the lack of movement or inclination are also factors that enable the development of these lesions[23-26]. As far as hospitalization, the result reflects what was observed in (Nicholson et al., 1988) in which it has been shown that the incidence of pressure ulcers is inversely related to the amount of movement performed at night in PD patients, whereby this factor notably increased in those individuals with PD and who also suffered from another comorbidity, such as dementia. Finally, this entails a series of medical implications regarding the treatment that is to be applied, causing the length of

hospital stay to be prolonged for a greater period of time as opposed to those who do not exhibit this comorbidity.

## *Impact and development of other comorbidities in Parkinson's disease patients and hospitalization days*

In an in-depth analysis of the study, the history and presence of the studied comorbidities would be of great interest, since in some cases, PD patients are susceptible to developing other diseases that can become high-risk comorbidities thus prolonging the length of stay hospital, as observed in PD patients with pneumonia or sacral ulcer. However, analyzing the cases where comorbidities have a lower relationship average with regards to the length of hospital stay mean implies knowing the background that lead to said situation. In our study, among the comorbidity cases that presented a significant difference below the mean were the cases of PD patients with hypothyroidism, AMI/dyslipidemia, and CET.

There is an association of PD patients who are suffering from hypothyroidism and a short hospital stay due to hormonal therapy with L-thyroxine to control the thyroid hormone (TH) levels since it reduces the motor symptoms of bradykinesia and Parkinson's hypomimia[27-29] which leads to the fact that development of hypothyroidism in PD patients can often go unnoticed, given that the course of both diseases implies similar clinical characteristics. When seen at the molecular level, it is suggested that a possible role of the thyroid gland and thyroperoxidase in the nitrosylation of serum proteins is what influences Parkinsonian nitrosative stress[30]. Therefore, the shorter hospital stay is directly related to the application of a TH treatment, such as the levothyroxine sodium, which reduces motor symptoms and it even has a potential effect with an oral solution dose of levodopa/carbidopa/ascorbic acid at hourly intervals[31].

In the case of AMI/Dyslipidemia, which are joint comorbidities that when they were present in PD patients in our study, it was observed that the hospital stay was shorter than the average in comparison when said comorbidity was not present. At an initial stage, AMI can be caused by dyslipidemia and it has already been studied that this condition represents a high risk factor in PD patients[32,33]. However, when said comorbidities are present to the point of needing hospitalization and resulting in a short length of stay, there is still no explanation for this. There may be different reasons where the medical treatment for AMI is mainly involved, such as the use of statins that is related to a protective effect against PD[34], which causes a speedy recovery in PD patients; however, it is still necessary to delve into this comorbidity and the relationships with the length of hospital stay of PD patients.

As far as the incidence of CET, it is known that this event places the individual at a risk zone of suffering from PD[35], in our case, the patients were already suffering from PD and in view of this comorbidity, it was observed that their length of hospital stay was short in contrast with PD patients who did not exhibit such comorbidity, thus making it necessary to thoroughly find out the medical treatment that was administered or the level of trauma and thus analyze the ways in which the patient would have a speedy recovery, in addition to following up given the fact that CETs imply a susceptibility to ischemic stroke that can exacerbate the stage of PD in patients[36].

It is important to note that in terms of the other comorbidity factors, also known as typical average diseases that appear during the 1st years of the disease such as diabetes mellitus, joint diseases, and fractures, although they are related to PD, an increase in comorbidity cannot be found until a after period of 10-15 years[13]. On the contrary, other intercurrent diseases such as pneumonia or cardiovascular diseases are the main cause of death[17,18].

Moreover, one of the observations that have been studied is the appearance of infectious diseases or their severity in PD patients[37]. Infections that affect the central nervous system (CNS) and sepsis are good research candidates because they can affect the risk of having or exacerbating PD, since pathological effects such as intense fever, inflammatory vascular alterations, or coagulation activation can cause the death of dopaminergic neurons leading to a severe PD process[38-40].

## *Context and limitations*

The present study must be contextualized within the COVID-19 pandemic, where it has been seen that there is a high mortality rate in patients with neurological impairment[41,42-44]. In the results of our patients, we have not found neurological impairment; however, these results could vary in a post-pandemic scenario, so in the following sections, we will address key points as to why the pandemic may not have an impact on the comorbidities found in Parkinson's patients.

Castillo et al. 2021[41] found patients with Parkinson's disease among the comorbidities of COVID-19, it should be noted that, in this research, suffering from Parkinson's disease was not a risk factor for death or hospital admission, in our study, none of the patients who were admitted as a hospital admission due to COVID-19. In contrast to another Mexican study, on COVID-19[43] and comorbidities, it was observed that the mean age was 51 years, as well as the comorbidities in patients with COVID-19 for hospitalization and death were: Systemic arterial hypertension and transplant. This age and comorbidities do not correspond to our patients, since 83.8% are over 60 years of age, as expected in patients with PD, and none of our comorbidities coincide with those of the study. These arguments suggest that Parkinson's disease patients in the present study were hospitalized for comorbidities other than COVID-19. We attribute this phenomenon, in which Parkinson's patients do not usually present COVID-19 as a hospital admission (at least in our hospital), to their motor disability, since, for this reason, they may not leave the house and in this way, its contagion is rare.

The main limitation of this study consisted of a small number of the population, despite the fact that all the patients in the database were taken; however, in the future publications, a multicenter study will be carried out to avoid this bias. It was impossible to establish a control group, since, if they had not had comorbidity, they would not have been hospitalized and would have been excluded from the study, perhaps in the future a control group of patients with PD without comorbidity who were hospitalized for an exacerbation of the disease could be added. Same Parkinson's disease will be compared with the mean days of hospitalization in patients with PD plus comorbidity who are hospitalized.

## Conclusion

Fourteen comorbidities were found in PD. Patients with sacral ulcer and pneumonia are hospitalized for a longer period of time in comparison to the different comorbidities. Special attention and care in preventing/treating these pathologies are recommended to reduce the number of hospitalization days, such that complications related to a prolonged stay and consequently, a reduction in resources spent on PD patients will be avoided.

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## Conflicts of interest

None.

## Ethical disclosures

**Protection of people and animals.** The authors declare that no experiments have been performed on humans or animals for this research.

**Data confidentiality.** The authors declare that no patient data appear in this article.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

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