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ORIGINAL ARTICLE

Psychiatric and somatic co-morbidities in patients with Parkinson's disease: A STROBE-compliant national multi-center, cross-sectional, observational study COSMOS in Slovakia

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Abstract

OBJECTIVE: Co-morbidities in any disorder can complicate its diagnostic process, they require more complex clinical management and lead to worse health outcomes and increased healthcare costs. There are regional differences in the prevalence of specific co-morbidities in Parkinson's disease (PD), and data from middle Europe are lacking. The project COSMOS aimed to disclose the prevalence of co-morbidities among patients with PD in Slovakia.

METHODS: In a national, multi-center, cross-sectional, observational study, neurologists gathered relevant demographical and clinical data aimed at all psychiatric and somatic co-morbidities.

RESULTS: From overall 737 patients, 51.00 % had at least one psychiatric co-morbidity, the most prevalent were depressive episode/recurrent depressive disorder (26.05%), sleep disorders (23.20%), dementia (13.16%), and neurotic, stress-related, and somatoform disorders (11.53%). In addition, 92.9 % had at least one somatic co-morbidity, the most prevalent were hypertensive diseases (67.71%), ischemic heart diseases (42.74%), diseases of the musculoskeletal system, and connective tissue (39.21), and disorders of lipoprotein metabolism (33.24%). The number of psychiatric co-morbidities increased with PD progression; the prevalence of somatic comorbidities increased also with the age ($p<0.001$ in all cases).

CONCLUSION: This study with a large cohort of PD patients confirmed a high prevalence of depression, dementia, sleep problems, and anxiety disorders, together with cardiovascular disorders, diseases of the musculoskeletal system, and metabolic syndrome. With PD progression, the number of both psychiatric and somatic co-morbidities is on the increase. If not treated properly, they lead to more complicated management. That's why it's essential to search for any

co-morbidity to provide patients with early and adequate therapy to avoid further worsening of quality of life.

Abbreviations:

PD	- Parkinson disease
QoL	- quality of life
ICD	- International Classification of Diseases

BACKGROUND

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder progressively leading to patients' disability. However, when treated properly, PD itself does not significantly shorten life expectancy compared to the general population (Hobson, Meara, and Ishihara-Paul 2010). As the largest incidence is among elderly patients, PD is often accompanied by various co-morbidities typical for advanced age. Nevertheless, some specific conditions are reported to be more frequent among PD patients compared to non-PD subjects of similar age. They can be linked to an intrinsic PD pathology (e.g., sleep disorders, depression, and pain), dopamine-replacing treatment (impulse control disorders, levodopa-induced peripheral neuropathy) or they can have a similar genetic basis (schizophrenia, Crohn's disease)(Nalls *et al.* 2014).

Somatic co-morbidities influence the life expectancy of PD patients more evidently. Doi *et al.* disclosed that cerebrovascular diseases, diabetes mellitus, malignant neoplasm, and heart diseases are the most frequent internal contributory causes of death in Japanese PD patients (Doi *et al.* 2011). On the other hand, psychiatric co-morbidities might deteriorate patients' quality of life (QoL). Both conditions increase the costs necessary to manage them (Bach *et al.* 2012). Polypharmacy is also a significant problem among PD patients with co-morbidities (McLean *et al.* 2017).

There are studies examining co-morbidities in PD in several countries, but to our knowledge, there are no published data from a Central European population. As result, the „COSMOS" project (CO-morbiditieS in MOst Severe Neurology & Psychiatric Disorders in Slovakia) was designed to map the prevalence and impact of co-morbidities among Slovak patients with the most frequent neurological and psychiatric conditions - Parkinson's and Alzheimer's disease, depression, schizophrenia, and bipolar affective disorder. It was aimed to improve diagnosis, treatment and prevention of co-morbidities in specialized outpatient departments.

The objective of this publication is to reveal data about the prevalence of psychiatric and somatic co-morbidities in a cohort of patients with idiopathic PD.

METHODS

In this national, multi-center, cross-sectional, observational study, random consecutive non-institutionalized patients with idiopathic PD according to the MDS diagnostic criteria (Postuma *et al.* 2015) were enrolled. The study was approved by the Ethics Committee of the Kosice Self-Governing Region (Namestie Maratonu mieru 1, 042 66 Kosice, Slovakia). The patients/participants provided their written informed consent to participate in this study. Informed consent was obtained from the legal guardian in case patients were not able to give them by themselves. The investigation was performed according to the Declaration of Helsinki.

After obtaining informed consent, we gathered all relevant demographical and clinical information:

- age,
- gender,
- PD duration,
- Hoehn and Yahr staging,
- presence of any psychiatric and somatic co-morbidity according to the International Classification of Diseases - ICD-10 (the co-morbidity was considered "present" only when it was currently and adequately managed by general practitioners, neurologists, or appropriate specialists (cardiologist, psychiatrist, etc.).

Subjects were examined by 38 neurologists of secondary and tertiary neurological centres from all regions of Slovakia by an on-line questionnaire developed for the COSMOS study.

The data were analysed with the IBM® SPSS Statistics® 22 software. Descriptive statistics were used to evaluate demographic and clinical data. Categorical parametric data were presented as percentages. Continuous parametric data satisfying normal distribution were described as mean ± standard deviation. If the data were non-normally distributed, they were described as median values with their corresponding interquartile. Correlation analysis of the data was conducted with the Spearman correlation test and linear regression. Using the Bonferroni approach to control for Type I error, a p-value ≤ .001 was required for statistical significance.

RESULTS

We examined 737 patients with idiopathic PD; 51.70% were female. All the demographic data are in Table 1.

From overall 737 patients, 95.4% had at least one co-morbidity. The number of all co-morbidities was predicted by higher age, and Hoehn & Yahr staging (p<0.001 in both cases).

From all subjects, 51.00 % had at least one psychiatric co-morbidity, the most prevalent were:

- depressive episode/recurrent depressive disorder (26.05%),
- sleep disorders (23.20%),

Tab. 1. Demographic data

	age (years)	Hoehn & Yahr staging	disease duration (years)
Mean	71.26	-	5.17
Median	-	2.00	-
Standard deviation	9.25	-	3.80
Minimum	33.00	1.00	1.00
Maximum	95.00	5.00	22.00

- dementia (13.16%),
- neurotic, stress-related and somatoform disorders (11.53%).

All the other psychiatric co-morbidities were below 10% (Figure 1).

The number of psychiatric co-morbidities was predicted by higher Hoehn & Yahr staging (p<0.001). From the most frequent psychiatric co-morbidities, only dementia was predicted also by higher age (p<0.001).

From overall 737 patients, 92.9 % had at least one somatic co-morbidity, 74.9% had two or more co-morbidities (median 3, minimum 0, maximum 9). The most prevalent were:

- hypertensive diseases (67.71%),
- ischemic heart diseases (42.74%),
- diseases of the musculoskeletal system and connective tissue (39.21%),
- disorders of lipoprotein metabolism and other lipidaemias (33.24%),
- diabetes mellitus (19.81%),
- diseases of the genitourinary system (17.77),
- peripheral vascular disorders (13.43%),
- stroke (10.18%).

All the others were below 10% (Figure 2).

A higher number of somatic co-morbidities was predicted by higher age and Hoehn & Yahr stage (p<0.001 in both cases).

DISCUSSION

Data about the prevalence of specific somatic and psychiatric co-morbidities of PD varies significantly due to different regions, population selection, and methodology being used. However, it is a fact that all co-morbidities increase morbidity and mortality, and decrease the QoL life of patients with PD. According to the PRIAMO study, 98.6% of patients with PD reported the presence of nonmotor symptoms - as a part of clinical presentation of PD itself (Barone *et al.* 2009). We report data from the middle-European region about the prevalence of specific disorders according to ICD-10 (treated separately by neurologist or other specialist) and discuss the most prevalent psychiatric and somatic co-morbidities.

From overall 737 patients, more than half had at least one psychiatric co-morbidity. Depression was the most frequent (26.5%), which is lower compared to the prevalence reported in large cohort studies - 42.8% (Gage *et al.* 2003), or 46%, (Jones *et al.* 2012) respectively. However, we did not include patients with mild depressive symptoms (as a possible part of PD presentation) not requiring treatment. Neither we considered patients treated with antidepressants in an indication other than depression (insomnia, chronic headache, or neuropathic pain). Nuti *et al.* (Nuti *et al.* 2004) disclosed that among non-fluctuating non-demented PD patients, 21.1% had major depression, which is more similar to the results of our study.

Clinically relevant anxiety-related disorders were present in more than 11% of patients which is lower than previously confirmed to be 24.5%–46.7% (Broen *et al.* 2016). The reason for relatively low prevalence could be the same as in depression – we included only patients diagnosed and treated with anxiety disorder, not those presenting with PD-related anxiety symptoms.

The prevalence of sleep disorders varies widely from 22% (Porter, Macfarlane, and Walker 2008) to 96.5% (Sobreira-Neto *et al.* 2017) according to the methodology used in different studies. In our population, 23.2% of patients were treated for problems with sleep. It is necessary to stress out that sleep disorders remain underestimated and underdiagnosed because they may not be routinely screened in daily clinical practice.

According to a large German study, 26.6% of patients with PD over the age of 65 have dementia (Riedel *et al.* 2016). We found the prevalence to be 13.16% in our population, where also younger patients with less severe PD were included. In our cohort, only dementia was linked to the age of subjects.

The number of other psychiatric co-morbidities correlated only with the Hoehn & Yahr staging, reflecting the fact that they might be independently associated with PD pathology and/or antiparkinsonian treatment.

The number of somatic co-morbidities was associated with both PD severity (Hoehn and Yahr staging) and patients' age. Of all subjects, 92.9% had at least one somatic co-morbidity; almost three-quarters of subjects had more than one co-morbidity.

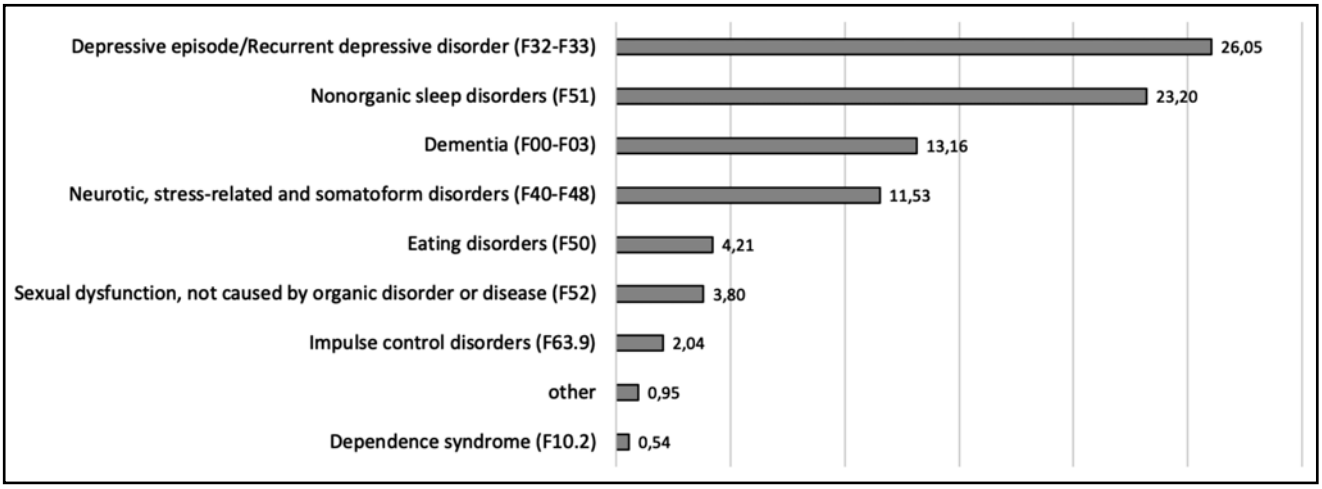

Fig. 1. Prevalence of psychiatric co-morbidities in Parkinson's disease

We detected a relatively high prevalence of hypertension among patients with PD – 67.71% patients with hypertension compared to 36% of patients with all heart/circulatory disorders reported in a large cohort of patients with PD by Jones *et al.* (Jones *et al.* 2012). The problem of blood pressure in PD is more complex than in the general population – with disease progression, we have to deal with typical orthostatic hypotension and nocturnal/supine hypertension. These opposing conditions generally do not respond to conventional antihypertensive therapy and require a more tailored treatment. As we often see in clinical practice, patients are treated for high blood pressure by general practitioners or cardiologists regardless of the presence of orthostatic hypotension. Although the latter is associated with a higher risk of syncope, cognitive problems, and/or falls, specialists usually prefer to deal with hypertension, as it may put patients at a higher risk of serious cardio- and cerebrovascular complications. Nevertheless, we consider this as a reason for the higher prevalence of hypertension in our population.

Musculoskeletal pain is a common symptom of PD (Valkovic *et al.* 2015) and we disclosed that diseases of the musculoskeletal system are the third most common somatic co-morbidity in our patients (almost 40%). Jones *et al.* (Jones *et al.* 2012) disclosed that arthritis alone (with no distinction between osteoarthritis and rheumatoid arthritis) was present in 46.6% of subjects of their PD cohort. Half of the cases reported only minimum pain in joints, hips, knees, shoulder, and spine, so the number of patients requiring treatment might have been lower.

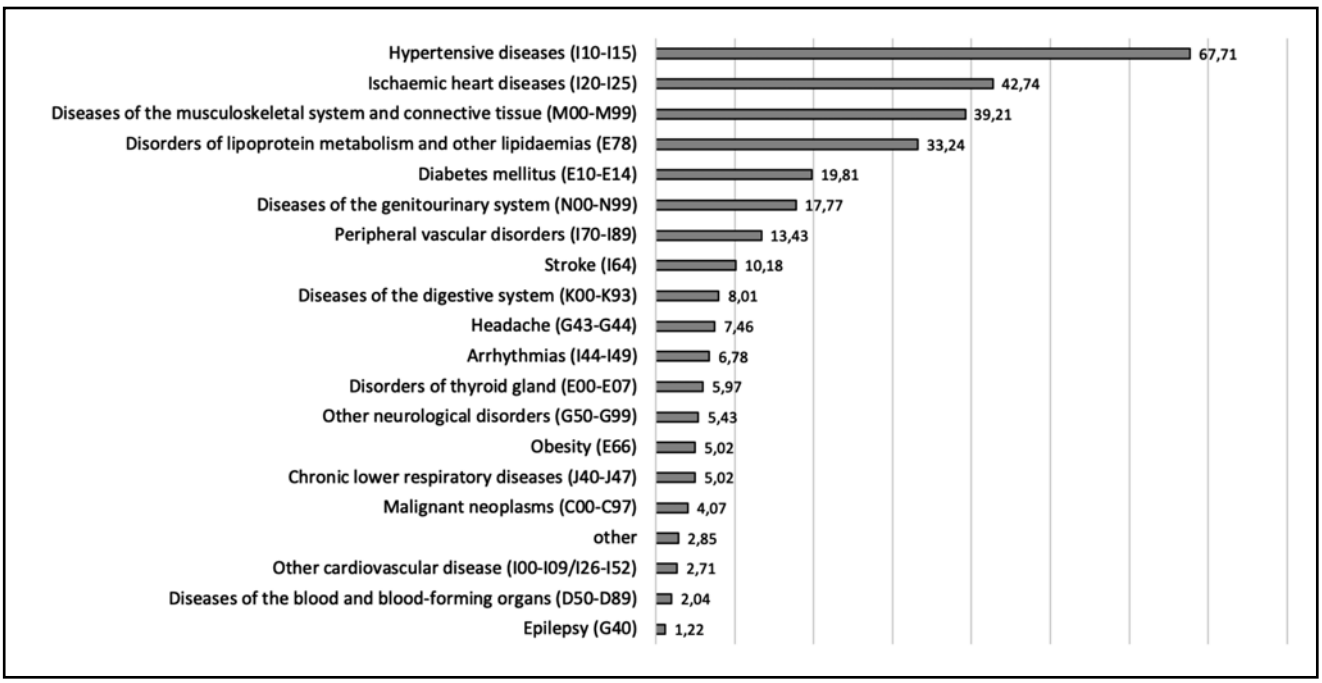

Fig. 2. Prevalence of somatic co-morbidities in Parkinson's disease

The prevalence of diabetes among patients with PD was confirmed to be higher than in the general population, however, the results vary to a great extent (Santiago, Bottero, and Potashkin 2017). Our data confirmed the high prevalence of both diabetes and metabolic syndrome, these data are similar to the prevalence in the general population of Slovakia (Mokán *et al.* 2008).

A limitation of our study might be the consecutive enrolment of the patients and higher preponderance of female gender in our cohort what could lead to slightly bias results. We also did not assess the severity of individual comorbidities or if they are affected by antiparkinsonian medication.

CONCLUSION

Our study disclosed that the most frequent psychiatric co-morbidities of PD in Slovakia are depression and anxiety disorders, sleep problems, and dementia. The prevalence of almost all of them was lower compared to other studies. We did not focus on PD-related neuropsychiatric symptoms, but we include only patients diagnosed and/or treated with specific disorders (according to the ICD-10). Nevertheless, we still consider psychiatric symptoms and disorders under-diagnosed in our population. Patients are often not willing to report them spontaneously, that's why is essential to search for any co-morbidity actively. Together with adequate treatment of the most common somatic co-morbidities – cardiovascular disorders, diseases of the musculoskeletal system, and metabolic syndrome – we might be able to reduce overall morbidity, mortality and avoid further worsening of quality of life in patients with PD.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Ethics Committee of the Kosice Self-Governing Region (Namestie Maratonu mieru 1, 042 66 Kosice, Slovakia). The patients/participants provided their written informed consent to participate in this study. Informed consent was obtained from the legal guardian in case patients were not able to give them by themselves. The investigation was performed according to the Declaration of Helsinki.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors have no conflicts of interest to declare.

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AUTHORS' CONTRIBUTIONS

Conception and design of the work: PV, JD.
Acquisition of data: MM
Analysis and interpretation of data: MM, JD, PV.
Drafting and/or revising the article: MM, JD, PV.
Final approval of the version to be published: MM, JD, PV.

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