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The diabetic parkinsonian – the association of diabetes mellitus comorbidity and symptoms of Parkinson's disease

Parkinsonik z cukrzycą – wpływ współchorobowości na przebieg choroby Parkinsona


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Abstract

Introduction and objective: Many studies have investigated the interplay between Parkinson's disease and diabetes mellitus, suggesting that glucose metabolism impairment may worsen the clinical course of Parkinson's disease. This study aimed to explore the association between diabetes mellitus and the course of Parkinson's disease. **Materials and methods:** A retrospective study was performed by analysing the clinical data of patients diagnosed with Parkinson's disease who were hospitalised in University Clinical Centre of the Medical University of Silesia from 2019 to 2021. The study group comprised 241 patients selected according to the study's inclusion and exclusion criteria. Their clinical conditions were assessed using body mass index, the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS), the Hoehn-Yahr scale, Mini-Mental State Examination (MMSE), Clock Drawing Test (CDT) and Beck Depression Inventory (BDI). Data were collected on current anti-parkinsonian treatment, fasting glycaemia, lipid panel, and thyroid stimulating hormone, homocysteine and vitamin D₃ levels. **Results:** The study group included 31 patients diagnosed with diabetes mellitus and 240 patients without glucose metabolism impairment. Both groups were matched by considering age, disease duration, and gender distribution. Diabetic patients displayed a higher MDS-UPDRS part III OFF rating (42 [31–55] vs. 48 [39–59]; $p = 0.0043$), higher MDS-UPDRS part III ON rating (17 [11–26] vs. 26.5 [19–32]; $p = 0.0009$) and higher BDI score (7 [4–11] vs. 11 [9–16]; $p = 0.0013$). As expected, patients with diabetes mellitus had a higher fasting glycaemia, total cholesterol, lower high-density lipoprotein cholesterol and higher body mass index. **Conclusions:** Our study confirms the relationship between diabetes mellitus and a worse clinical course for Parkinson's disease.

Keywords: Parkinson's disease, diabetes mellitus, glucose metabolism impairment

Streszczenie

Wprowadzenie: Liczne badania wskazują na współzależność między chorobą Parkinsona a cukrzycą. Sugerują, że zaburzenia metabolizmu glukozy mogą pogarszać przebieg kliniczny choroby Parkinsona. Celem badania była ocena związku między cukrzycą a przebiegiem choroby Parkinsona. **Materiał i metody:** Przeprowadzono retrospektywną analizę danych medycznych pacjentów z rozpoznaną chorobą Parkinsona hospitalizowanych między 2019 a 2021 rokiem w Uniwersyteckim Centrum Klinicznym w Katowicach. Grupa badana składała się z 241 pacjentów wybranych zgodnie z kryteriami włączenia i wyłączenia z badania. W ocenie pacjentów zastosowano wskaźnik masy ciała, Ujednoliconą Skalę Oceny Choroby Parkinsona (Movement Disorder Society Unified Parkinson's Disease Rating Scale, MDS-UPDRS), skalę Hoehn-Yahra, Krótką Skalę Oceny Stanu Umysłowego (Mini-Mental State Examination, MMSE), Test Rysowania Zegara (Clock Drawing Test, CDT) i Skalę Depresji Becka (Beck Depression Inventory, BDI). Zebrano informacje o stosowanym leczeniu choroby Parkinsona, glikemii na czczo, profilu lipidowym, stężeniu hormonu tyreotropowego, homocysteiny i witaminy D₃. **Wyniki:** 31 osób w grupie badanej miało rozpoznaną cukrzycę, natomiast u 240 osób nie zaobserwowano zaburzeń metabolizmu węglowodanów. Obie grupy były porównywalne pod względem wieku, czasu trwania choroby i płci. Pacjenci z rozpoznaną

cukrzycą cechowali się wyższym wynikiem w III części skali MDS-UPDRS w stanie OFF (42 [31–55] vs 48 [39–59]; $p = 0,0043$), wyższym wynikiem w III części skali MDS-UPDRS w stanie ON (17 [11–26] vs 26,5 [19–32]; $p = 0,0009$) oraz wyższym wynikiem BDI (7 [4–11] vs 11 [9–16]; $p = 0,0013$). Zgodnie z oczekiwaniami pacjenci z rozpoznaną cukrzycą mieli wyższe glikemię na czczo, stężenie cholesterolu całkowitego, cholesterolu LDL i wyższy wskaźnik masy ciała. **Wnioski:** Badanie potwierdziło związek współwystępowania cukrzycy z gorszym przebiegiem choroby Parkinsona.

Słowa kluczowe: choroba Parkinsona, cukrzyca, zaburzenia metabolizmu glukozy

INTRODUCTION

Diabetes mellitus (DM) and Parkinson's disease (PD) are considered epidemics in modern societies. A nationwide Norwegian study assessing the epidemiology of PD over a 12-year period (2005–2016) has shown that PD prevalence increases with time in all age groups, in a highly dynamic manner. The prevalence of PD in the population was, on average, 0.2% in females and 0.23% in males in the general population; in contrast, in the population aged >65 years, the PD prevalence is 0.98% in females and 1.35% in males (Brakedal et al., 2022). Worldwide trends indicate that the global prevalence of PD increased dramatically between 1990 and 2019 (Ou et al., 2021).

DM poses a considerable problem as well. Currently, about 422 million people worldwide have DM, and 1.5 million deaths are directly attributed to DM each year. The number of cases and the prevalence of DM have steadily increased over the past few decades (World Health Organization, 2016).

The interplay between PD and DM has been the subject of numerous studies. A large prospective study carried out in 2011 among older US adults showed that DM was associated with a modest increase in the risk of PD, and the risk increased significantly in those who had had the disease for more than 10 years (Xu et al., 2011). The association between PD with DM was revealed in other studies as well (Chmiela et al., 2022; Yang et al., 2017). Moreover, many studies in the literature have shown that impaired glucose metabolism may be a possible cause of dysautonomia, which commonly occurs in PD (Marques et al., 2018). DM and PD could also share some commonly dysregulated pathways, including those involved in the insulin response. Pancreatic insulin production and secretion are modulated by the autonomic nervous system (Rodriguez-Diaz et al., 2011), and the severity of dysautonomia in PD may be linked with blood glucose dysregulation.

It is thought that DM impacts the course of PD. Cereda et al. (2012) reported the findings of a case-control study of patients with PD with and without antecedent DM. They found the group with both PD and DM presented higher motor scores and received higher doses of levodopa (Cereda et al., 2012). These findings suggest that DM may exacerbate motor impairments. Similar results were observed in other studies (Pagano et al., 2018).

Although various authors have investigated the link between DM and PD, the issue remains unclear and requires

further research. Therefore, this study aimed to explore the impact of DM on the clinical features and course of PD by examining the associations between DM or prediabetes with the clinical characteristics and parameters of patients with PD.

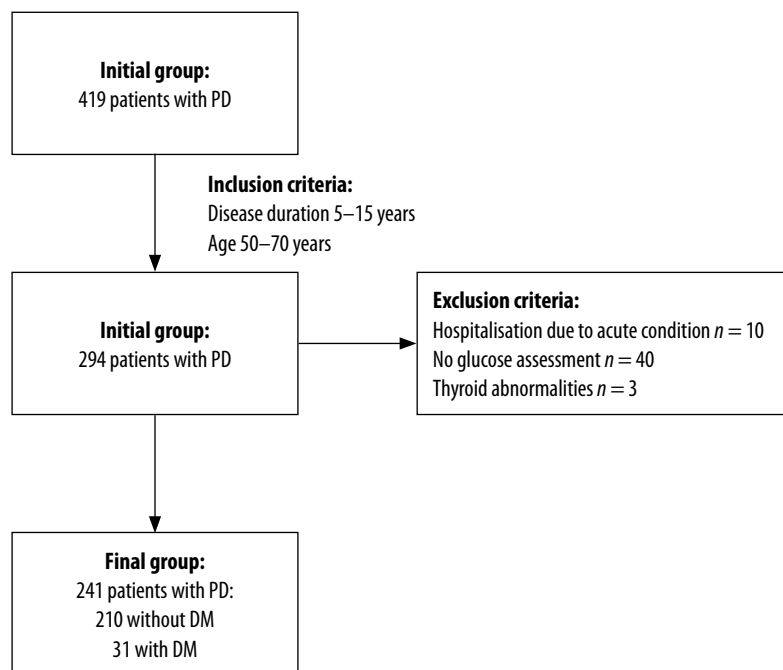
MATERIALS AND METHODS

We performed a cross-sectional retrospective study to assess the association between the severity of motor and non-motor symptoms of PD and type 2 DM comorbidity. The initial group consisted of all the patients admitted to the University Clinical Centre of the Medical University of Silesia from January 2019 to November 2021 with clinically confirmed PD according to the Movement Disorder Society (MDS) clinical diagnostic criteria (Siuda et al., 2020). Diagnoses were made by a neurologist experienced in the diagnostics and treatment of neurodegenerative diseases. In the next step, patients who met the inclusion criteria were selected from this group. The inclusion criteria were: age range of 50 to 75 years and disease duration of 5 to 15 years. Patients hospitalised due to acute conditions were excluded from this study. Other exclusion criteria comprised significant thyroid or hepatic disorder or absence of glycaemia assessment. The initial group consisted of 419 patients with diagnosed with PD; 294 met the inclusion criteria, 40 patients were excluded due to lack of glucose assessment, 10 were hospitalised due to an acute condition, and 3 had a significant abnormality in the thyroid assessment.

Then, the participants were divided into two groups:

1. patients with diagnosed type 2 DM based on their medical history or found during the analysis;
2. patients without a diagnosis of DM.

Type 2 DM was defined according to the recommendations of the American Diabetes Association (2021). The selection process and final group composition are presented in Fig. 1. The study group comprised 241 patients, including 93 females (39%) and 148 males (61%), aged 50–75 years (median 67 [60–73]). The clinical data of the final group of 241 patients were collected, including gender; age; body mass index (BMI); duration of the disease; assessment of motor status using part III of the MDS-UPDRS scale (Movement Disorder Society Unified Parkinson's Disease Rating Scale), performed without dopamine replacement therapy (DRT) and after administration of a dose of levodopa; and Hoehn-Yahr scale score. In addition, assessment of cognitive function using the Mini-Mental State Examination (MMSE)



PD – Parkinson's disease; DM – diabetes mellitus.

Fig. 1. Final group creation process

and Clock Drawing Test (CDT) and the Beck Depression Inventory (BDI) results were gathered. Data on current anti-parkinsonian treatment were also collected. An analysis of the patients' laboratory results including fasting glycaemia, lipid metabolism, thyroid function, and homocysteine was performed.

The statistical analysis was performed with the Statistica 13.3 software system (TIBCO Software Inc., 2017; <http://statistica.io>). The quantitative variables are presented as arithmetic means and standard deviations (normally distributed variable) or medians and interquartile ranges (variables with skewed distribution). The qualitative variables are expressed as absolute values and percentages. The normality of distribution was assessed with the Shapiro–Wilk test.

Due to a lack of confirmation of the normal distribution in the analysed groups, the intergroup differences for the quantitative variable were assessed with the Mann–Whitney *U*-test, Fisher's exact test or chi-square test. A *p*-value below or equal to 0.05 was considered statistically significant. Odds ratios (ORs) with a 95% confidence interval (CI) and *p* values were obtained using binary logistic regression. The variables that were significantly associated with the univariate logistic regression were then analysed using multivariate logistic regression. The final predictive model for DM was fitted using the forward stepwise selection method. The significance level was set at *p* < 0.05.

Due to the retrospective character of the work and data anonymisation, the Medical University of Silesia Ethics Committee waived the requirement to obtain ethical approval for this study.

RESULTS

Comparison of characteristics of PD patients with and without diabetes

In the study group, 31 patients (15%) were diagnosed with DM. The groups of patients were matched for age, Hoehn–Yahr scale, and disease duration. The patients with DM were characterised by a higher BMI (26.0 [24.1–29.2] vs. 28.4 [22.7–30.5] kg/m²; *p* = 0.001), while patients without DM were characterised by a higher levodopa equivalent daily dose (LEDD) (1,150 [710–1,220] vs. 1,050 [601–1,220]). The detailed data are provided in Tab. 1.

Diabetes and motor status

The patients diagnosed with DM were characterised by a worse motor status both in the OFF (MDS-UPDRS p. III OFF 42 [31–55] vs. 48 [39–59]; *p* = 0.0043) and ON (MDS-UPDRS p. III ON 17 [11–26] vs. 26.5 [19–32]; *p* = 0.0009) states. The detailed data are provided in Tab. 2.

Diabetes and non-motor symptoms

The patients diagnosed with DM had significantly worse BDI scores (7 [4–11] vs. 11 [9–16]; *p* = 0.0013). There were no differences between the analysed groups regarding cognitive function (MMSE and CDT). The detailed data are provided in Tab. 3.

	Non-diabetic n = 210	Diabetic n = 31	p-value
Age [years]	67 [60–73]	67 [60–73]	0.5434
Gender • Female • Male	79 (37.7%) 131 (62.3%)	14 (45.2%) 17 (54.8%)	0.2696
Hoehn–Yahr scale	3 [2.5–3]	3 [2.5–3]	0.2901
LEDD [mg]	1150 [710–1,660]	1,050 [601–1,220]	0.0400
Duration of the disease [years]	10 [8–12]	10 [8–12]	0.5102
BMI [kg/m ²]	26.0 [24.1–29.2]	28.4 [22.7–30.5]	0.0012
BMI – body mass index; LEDD – levodopa equivalent daily dose.			

Tab. 1. Group characteristics of patients with Parkinson's disease with and without a diagnosis of diabetes. Statistical analyses were performed using Mann–Whitney U-test, Fisher's exact test or chi-square test

	Non-diabetic n = 210	Diabetic n = 31	p-value
MDS-UPDRS part III OFF	42 [31–55]	48 [39–59]	0.0432
MDR-UPDRS part III ON	17 [11–26]	26.5 [19–32]	0.0099
Δ MDS-UPDRS part III [%]	54.8 [43.6–68.2]	23 [16–29]	0.1241
MDS-UPDRS – Movement Disorder Society Unified Parkinson's Disease Rating Scale.			

Tab. 2. MDS-UPDRS part III results of patients with Parkinson's disease with and without a diagnosis of diabetes. Statistical analyses were performed using Mann–Whitney U-test

	Non-diabetic n = 210	Diabetic n = 31	p-value
MMSE	26 [24–28]	26 [22–28]	0.5843
CDT	9 [8–10]	9,5 [6–10]	0.5187
BDI	7 [4–11]	11 [9–16]	0.0013
BDI – Beck Depression Inventory; CDT – Clock Drawing Test; MMSE – Mini-Mental State Examination.			

Tab. 3. MMSE, CDT and BDI results of patients with Parkinson's disease with and without a diagnosis of diabetes. Statistical analyses were performed using Mann–Whitney U-test

Diabetes and laboratory results

As expected, the groups differed in their fasting glycaemia levels (99 [88–111.5] vs. 122 [107–160.5]; $p = 0.000$). The patients with DM displayed lower high-density lipoprotein (HDL) cholesterol levels (59.8 [51–68] vs. 48.5 [40.7–58]; $p = 0.0012$) and higher triglycerides levels (78 [62.2–107] vs. 103 [75.5–146]; $p = 0.0056$). There were no differences in homocysteine, vitamin D₃, total cholesterol, and low-density lipoprotein (LDL) cholesterol levels. The detailed data are provided in Tab. 4.

Multivariable logistic regression analysis was performed based on the univariate logistic regression results. The best predictive model identified DM as a predictor for a higher BDI score (OR 1.40 [1.02–1.62]; $p = 0.002$) and higher MDS-UPDRS p. III ON score (OR 1.63 [1.26–2.7]; $p = 0.049$). The results of the logistic regression analysis are summarised in Tab. 5.

The second model was performed to assess the correlations between PD dementia (PDD), defined by MMSE score <24 and cognitive dysfunction that interferes with the activities of daily living and motor and non-motor symptoms of PD. The best predictive model identified PDD as a predictor

of worse MDS-UPDRS p. III ON (OR 0.06 [0.02–0.10]; $p = 0.001$) and BDI score (OR 0.134 [0.06–0.21]; $p = 0.000$). The results of the logistic regression analysis are summarised in Tab. 5.

DISCUSSION

The co-occurrence of DM poses a considerable treatment challenge for many patients with PD due to the complex nature and more severe clinical course of the disease. In 1993, Sandyk demonstrated an interplay between PD and type 2 DM, evidencing that up to 50–80% of patients with PD had altered glucose tolerance in response to a glucose load. Since then, intense research has been conducted to explain this association. For instance, Xu et al. (2011) proved that diabetes was a risk factor for PD and increased the risk of developing this neurodegenerative condition by up to 41%. A large, population-based, cross-sectional study by De Pablo-Fernandez et al. in 2017 found no significant association between diabetes and PD, although a positive association between PD and long-duration diabetes (over ten years) was noted. However, in another retrospective cohort study conducted by the same authors,

	Non-diabetic n = 210	Diabetic n = 31	p-value
Total cholesterol [mg/dL]	202 [171–233]	190 [142–222]	0.1523
HDL cholesterol [mg/dL]	59.8 [51–68]	48.5 [40.7–58]	0.0012
LDL cholesterol [mg/dL]	125.4 [94–155.8]	107.4 [77–150.5]	0.1900
Triglycerides [mg/dL]	78 [62.2–107]	103 [75.5–146]	0.0056
Homocysteine	16.1 [11.6–17.4]	17.9 [12.7–21.2]	0.0850
Vitamin D ₃ [ng/mL]	24 [16–35]	26.7 [12.3–36.5]	0.7433
Fasting glycaemia [mg/dL]	99 [88–111.5]	122 [107–160.5]	0.0000
TSH – thyroid stimulating hormone; LDL – low-density lipoprotein; HDL – high-density lipoprotein.			

Tab. 4. Demographic, clinical, and laboratory characteristics of the study group with and without a diagnosis of diabetes. Statistical analyses were performed using Mann–Whitney U-test, Fisher's exact test or chi-square test

	OR	95% CI		p
BDI	1.379	1.024	1.623	0.002
MDS-UPDRS p. III ON	1.631	1.256	2.670	0.049
BDI – Beck Depression Inventory; DM – diabetes mellitus; CI – confidence interval; MDS-UPDRS – Movement Disorder Society Unified Parkinson's Disease Rating Scale; OR – odds ratio.				

Tab. 5. Results of logistic regression using DM as a predictor of the analysed variables

	OR	95 CI		p
MDS-UPDRS p. III ON	0.061	0.024	0.098	0.001
BDI	0.134	0.056	0.2127	0.000
BDI – Beck Depression Inventory; CI – confidence interval; MDS-UPDRS – Movement Disorder Society Unified Parkinson's Disease Rating Scale; OR – odds ratio.				

Tab. 6. Results of logistic regression using the presence of Parkinson's disease dementia as a predictor of the analysed variables

a link between these two conditions was shown, and the effects were stronger in patients with type 2 DM who were younger or suffered from complications of DM (De Pablo-Fernandez et al., 2018). Our study, comparing patients with PD with and without DM, matched for disease duration, age and sex, confirms the association between the coexistence of PD and DM and the greater severity of PD symptoms. Furthermore, another retrospective cohort study described a significant association between impaired fasting glycaemia and synucleinopathies (mainly in patients with PD) compared to those not associated with alpha-synuclein parkinsonism (Chmiela et al., 2022). This suggests that patients with PD should have their glycaemia monitored carefully. The conclusion is also supported by an investigation performed by Marques et al. (2018) who conducted oral glucose tolerance tests (OGTTs) in patients with PD and healthy controls. The blood glucose levels measured at 90 and 150 minutes were much higher in patients with PD. On the other hand, this observation was not related to plasma insulin and urinary glucose levels during the whole test. Notably, impaired glucose levels were strongly associated with a longer duration of PD (with a correlation coefficient of 0.13 – 95% CI 0.05–0.17) and severity of dysautonomia, measured using the Scale for Outcomes in PD-Autonomic (SCOPA-AUT) (with a correlation coefficient of 1.48 – 95% CI 0.27–2.7) (Marques et al., 2018). In addition, there are many other studies in which a dependence between DM and PD has been observed (Chung et al., 2021; De Pablo-Fernandez et al., 2018).

Furthermore, there is some evidence that DM may affect the course of PD. Some research suggests that DM exacerbates motor dysfunction. Cereda et al. (2012) characterised 178 patients divided into two groups, matched for gender, BMI and duration of PD. They showed that the coexistence of DM and PD predisposed to higher doses of levodopa equivalent (mean 4.5 mg/kg/day in patients without DM and 6.5 mg/kg/day in patients with DM; $p < 0.0001$) (Cereda et al., 2012). In our study, however, diabetic patients were taking lower doses of antiparkinsonian drugs (median LEDD 1,150 mg [710–1,660] in patients without DM and 1,050 mg [601–1,220] in patients with DM; $p = 0.04$). Furthermore, Cereda et al. (2012) showed significantly higher Hoehn–Yahr staging ($p = 0.009$) and Unified Parkinson's Disease Rating Scale (UPDRS) scores in parts I–III ($p = 0.024$). This study did not confirm the relationship between diabetes and a higher degree of PD severity (according to the Hoehn–Yahr scale). However, it should be remembered that the study group was selected to minimise the influence of factors such as age and duration of the disease. Nevertheless, this study confirmed the relationship between the coexistence of symptoms and the greater severity of PD symptoms.

Our study supports previous research, showing a link between PD and diabetes. This research demonstrated that patients with DM had higher UPDRS-III scores in both ON ($p = 0.0099$) and OFF ($p = 0.0432$) states compared to those without DM. Another investigation that corroborated these results found that patients with PD and DM had significantly

higher UPDRS-III scores compared to patients with PD and two control groups without PD (with or without DM) ($p < 0.01$). Additionally, the authors demonstrated the interplay between DM and significant striatal dopaminergic deficits using single-photon emission computed tomography (SPECT). Furthermore, patients with both PD and DM had higher cerebrospinal fluid tau levels (40.4 pg/mL in PD vs. 54.7 pg/mL in PD-DM; $p < 0.05$). On the other hand, there were important differences between the control groups in terms of cerebrospinal fluid (CSF) tau and α -synuclein levels ($p < 0.05$). The authors suggested that these data could indirectly explain the mechanism underlying the impact of impaired glucose metabolism on the course of PD, such as reduced neuronal survival (Pagano et al., 2018; Rhee et al., 2020). Some research findings have revealed that DM can be associated with postural instability and gait disturbance in PD, which may be relevant indications for rehabilitating therapies (Kotagal et al., 2013). Depression is one of the most frequent neuropsychiatric pathologies that are strongly related to PD. Its prevalence varies widely from 2.7% to 90% depending on the territory, the methodology, and the diagnostic criteria used (Reijnders et al., 2008). Depression has a negative impact on the quality of life in PD (Chuquilín-Arista et al., 2020). The other disease associated with this psychiatric problem is DM, which displays aetiological bi-directionality. Type 2 DM increases the risk of depressive episodes and contributes to a more severe course of depression, while depression increases the risk of the development of type 2 DM (Deischinger et al., 2020; Semenkovich et al., 2015). European studies estimate that depression occurs in over 30% of patients with PD (Chuquilín-Arista et al., 2020), while in the general population, the prevalence rate is about 6% (Arias-de la Torre et al., 2021). Nevertheless, it has already been evidenced using the Hamilton Anxiety Scale (HAS) and the Hamilton Depression Scale (HDS) that major depression (21.1%) and panic disorders (30%) are the most frequent psychiatric disorders in patients with PD ($p < 0.01$) (Nuti et al., 2004). In line with this information, DM coexisting with PD should be considered a risk factor for psychiatric disorders. Weber et al. (2000) reported higher cortisol levels in patients with depression than in controls. This finding could be connected to higher hypothalamic–pituitary–adrenal (HPA) axis activation, a pathogenic mechanism in depression and DM which may complicate their disease courses (Weber et al., 2000). However, not many studies have assessed the influence of DM on psychiatric symptoms in patients with PD (Bohnen et al., 2014; Riederer et al., 2011). Our study found out that DM could significantly affect psychiatric disorders, such as depression. The coexistence of diabetes was associated with a statistically higher score in the BDI. This indicated that there might be a particular sensitivity towards mood disorders in this group of patients.

An interplay between DM and a more severe stage of cognitive impairment in patients with PD has been reported (Bohnen et al., 2014; Pagano et al., 2018). However, this

study did not confirm the association between DM and cognitive impairment in PD. There were no differences in the results of the MMSE and CDT tests between the study groups. Nevertheless, it should be emphasised that the presence of cognitive disorders in our study was associated with worse motor status and greater depressive disorders.

As we expected, patients with DM had higher BMI ($p = 0.021$) and higher LDL cholesterol levels ($p = 0.001$), but lower HDL cholesterol levels ($p = 0.001$), which are risk factors for metabolic syndrome (Rochlani et al., 2017).

Our study has certain limitations. First of all, the patients with DM had some metabolic risk factors, which could impact their blood glucose levels and motor functions. Secondly, selection and sampling bias was possible due to the retrospective nature of this single-centre study. Additionally, due to the study's retrospective design, we could not objectivise the patients' examinations.

CONCLUSIONS

Our study results confirm the relationship between DM and a worse course for PD. A diagnosis of diabetes in PD patients was associated with worse motor status and higher BDI scores. Our study findings emphasise the significance of early treatment and careful glycaemic control of diabetic patients with PD, as the concomitance of these two diseases has a negative impact on the course of PD. Furthermore, it should be imperative for medical personnel to vigilantly screen patients with PD for mood disorders, especially those with coexisting DM. In the future, prospective, large-scale, multicentre studies are needed to elucidate these complex interactions.

Conflicts of interest

The authors declare no conflict of interest.

Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki. Ethical review and approval were waived for this study due to the retrospective character of the work and data anonymisation. The Ethics Committee of the Medical University of Silesia waived the requirement to obtain the ethical approval for this study.

Informed consent statement

Patient consent was waived due to the retrospective character of the work and data anonymisation.

Data availability statement

The data presented in this study are available on request from the corresponding author.

Author contribution

Original concept of study: TC, JWG, AG. Collection, recording and/or compilation of data: TC, JWG, DWil, DWak, AK. Analysis and interpretation of data: TC, JWG, DWil, DWak, AK, ACF. Writing of manuscript: TC, JWG, DWil, DWak, AK, ACF. Critical review of manuscript: TC, AG. Final approval of manuscript: TC, AG.

References

- American Diabetes Association: 2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes–2021*. *Diabetes Care* 2021; 44 (Suppl 1): S15–S33.
- Arias-de la Torre J, Vilagut G, Ronaldson A et al.: Prevalence and variability of current depressive disorder in 27 European countries: a population-based study. *Lancet Public Health* 2021; 6: e729–e738.
- Bohnen NI, Kotagal V, Müller MLTM et al.: Diabetes mellitus is independently associated with more severe cognitive impairment in Parkinson disease. *Parkinsonism Relat Disord* 2014; 20: 1394–1398.
- Brakedal B, Toker L, Haugarvoll K et al.: A nationwide study of the incidence, prevalence and mortality of Parkinson's disease in the Norwegian population. *NPJ Parkinsons Dis* 2022; 8: 19.
- Cereda E, Barichella M, Cassani E et al.: Clinical features of Parkinson disease when onset of diabetes came first: a case-control study. *Neurology* 2012; 78: 1507–1511.
- Chmiela T, Węgrzynek J, Kasprzyk A et al.: If not insulin resistance so what? Comparison of fasting glycemia in idiopathic Parkinson's disease and atypical parkinsonism. *Diabetes Metab Syndr Obes* 2022; 15: 1451–1460.
- Chung HS, Lee JS, Kim JA et al.: Fasting plasma glucose variability in midlife and risk of Parkinson's disease: a nationwide population-based study. *Diabetes Metab* 2021; 47: 101195.
- Chuquilín-Arista F, Álvarez-Avellón T, Menéndez-González M: Prevalence of depression and anxiety in Parkinson disease and impact on quality of life: a community-based study in Spain. *J Geriatr Psychiatry Neurol* 2020; 33: 207–213.
- De Pablo-Fernandez E, Goldacre R, Pakpoor J et al.: Association between diabetes and subsequent Parkinson disease: a record-linkage cohort study. *Neurology* 2018; 91: e139–e142.
- De Pablo-Fernandez E, Sierra-Hidalgo F, Benito-León J et al.: Association between Parkinson's disease and diabetes: data from NEDICES study. *Acta Neurol Scand* 2017; 136: 732–736.
- Deischer C, Dervic E, Leutner M et al.: Diabetes mellitus is associated with a higher risk for major depressive disorder in women than in men. *BMJ Open Diabetes Res Care* 2020; 8: e001430.
- Kotagal V, Albin RL, Müller MLTM et al.: Diabetes is associated with postural instability and gait difficulty in Parkinson disease. *Parkinsonism Relat Disord* 2013; 19: 522–526.
- Marques A, Dutheil F, Durand E et al.: Glucose dysregulation in Parkinson's disease: too much glucose or not enough insulin? *Parkinsonism Relat Disord* 2018; 55: 122–127.
- Nuti A, Ceravolo R, Piccinni A et al.: Psychiatric comorbidity in a population of Parkinson's disease patients. *Eur J Neurol* 2004; 11: 315–320.
- Ou Z, Pan J, Tang S et al.: Global trends in the incidence, prevalence, and years lived with disability of Parkinson's disease in 204 countries/territories from 1990 to 2019. *Front Public Health* 2021; 9: 776847.
- Pagano G, Polychronis S, Wilson H et al.: Diabetes mellitus and Parkinson disease. *Neurology* 2018; 90: e1654–e1662.
- Reijnders JSAM, Ehrt U, Weber WEJ et al.: A systematic review of prevalence studies of depression in Parkinson's disease. *Mov Disord* 2008; 23: 183–189.
- Rhee SY, Han KD, Kwon H et al.: Association between glycemic status and the risk of Parkinson disease: a nationwide population-based study. *Diabetes Care* 2020; 43: 2169–2175.
- Riederer P, Bartl J, Laux G et al.: Diabetes type II: a risk factor for depression-Parkinson-Alzheimer? *Neurotox Res* 2011; 19: 253–265.
- Rochlani Y, Pothineni NV, Kovelamudi S et al.: Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. *Ther Adv Cardiovasc Dis* 2017; 11: 215–225.
- Rodríguez-Díaz R, Abdulreda MH, Formoso AL et al.: Innervation patterns of autonomic axons in the human endocrine pancreas. *Cell Metab* 2011; 14: 45–54.
- Sandyk R: The relationship between diabetes mellitus and Parkinson's disease. *Int J Neurosci* 1993; 69: 125–130.
- Semenkovich K, Brown ME, Svrakic DM et al.: Depression in type 2 diabetes mellitus: prevalence, impact, and treatment. *Drugs* 2015; 75: 577–587.
- Siuda J, Boczarska-Jedynak M, Budrewicz S et al.; MDS-UPDRS Polish Validation Task Force: Validation of the Polish version of the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS). *Neurol Neurochir Pol* 2020; 54: 416–425.
- Weber B, Schweiger U, Deuschle M et al.: Major depression and impaired glucose tolerance. *Exp Clin Endocrinol Diabetes* 2000; 108: 187–190.
- World Health Organization: Global report on diabetes. World Health Organization, Geneva 2016. Available from: <https://www.who.int/publications/i/item/9789241565257> [cited: 7 June 2022].
- Xu Q, Park Y, Huang X et al.: Diabetes and risk of Parkinson's disease. *Diabetes Care* 2011; 34: 910–915.
- Yang YW, Hsieh TF, Li CI et al.: Increased risk of Parkinson disease with diabetes mellitus in a population-based study. *Medicine (Baltimore)* 2017; 96: e5921.