

# Exploring the association between pain, demographic and clinical variables in Georgian patients with Parkinson's disease

GVANTSA KHODELI<sup>1</sup>, ALEKSANDRE TSKITISHVILI<sup>2</sup>, MARIAM GOLETIANI<sup>3</sup>,  
SOPHIA SOPROMADZE<sup>4</sup>, IRINE KHATIASHVILI<sup>3,5</sup> and MARIKA MEGRELISHVILI<sup>1,3</sup>

<sup>1</sup>School of Medicine, Ilia State University, Tbilisi 0179, Georgia; <sup>2</sup>Department of Internal Medicine, NYC Health + Hospitals/South Brooklyn Health, Brooklyn, NY 11235, USA; <sup>3</sup>Department of Neurology, Khechinashvili University Hospital, Tbilisi 0179, Georgia; <sup>4</sup>Faculty of Healthcare Sciences, East European University, Tbilisi 0182, Georgia; <sup>5</sup>Department of Clinical Neurology, Tbilisi State Medical University, Tbilisi 0186, Georgia

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**Abstract.** Pain is a frequent occurrence in Parkinson's disease (PD), with a reported prevalence of >80%. The first ever validated scale to assess pain in PD, the King's PD Pain Scale (KPPS), was developed in 2015. The present study aimed to evaluate the correlation between general demographic (age and sex) and PD-related characteristics (disease duration, cognitive function, anxiety, depression and disability) and the KPPS score in a patient population with PD. A total of 100 adult patients, aged 45-86 years, were assessed. The study measured the correlation between PD-related pain and age, time from disease onset, disability due to impaired mobility, depression severity, anxiety severity, cognitive function and PD severity, followed by multiple regression analysis to determine individual KPPS domain and total scores. Moderate, positive correlations were found between anxiety severity and the KPPS total score, and between disease severity and KPPS Domain 4 score. In addition, weak correlations were present between the following: Anxiety severity and KPPS Domain 1, 3, 4, 5 and 6 scores; age and KPPS Domain 3 score; disability due to impaired mobility and KPPS Domain 4 and KPPS total scores; depression and Domain 1, 4, 5, 7 and KPPS total scores. In multiple regression models, the anxiety score was found to be a predictor of Domain 1, 3, 4, 5 and 6, and KPPS total scores; the disease severity score was a predictor of Domain 4 score; impaired mobility predicted KPPS total score; and depression severity predicted Domain 1 score. Consistent with prior evidence, the correlation and predictive association between anxiety severity and PD-related

pain strongly suggest a cause-and-effect association. The association between depression and pain is inconsistently demonstrated and may be subtle and nuanced, although less likely causal. No association was found between KPPS and disease duration, cognitive function or sex. Further research is required regarding the association between clinical and demographical variables and PD-related pain.

## Introduction

Symptoms resembling Parkinson's disease (PD) have been described in ancient texts (1). However, it was first considered as a standalone disease by James Parkinson in 1817 (2). Currently, PD is the second most common neurodegenerative condition following Alzheimer's disease, has the most rapidly increasing prevalence among neurological disorders (3) and is projected to affect ~13 million individuals worldwide by the year 2040 (4). This disease places a substantial burden on the population of Georgia. In 2016, 5,900 patients were diagnosed with PD in the country, which represented an 8.6% change from the 1990 baseline (5).

Although extrapyramidal motor deficit is the hallmark of PD, pain is also very frequent during this disorder, with a prevalence of >80% reported by certain studies (6,7). Despite its ubiquity, the instruments used to assess PD-related pain have only begun to be developed recently. The first ever scale used to assess pain in PD was validated by Chaudhuri *et al* (8) in 2015 and is currently referred as the King's Parkinson's disease Pain Scale (KPPS).

The present study aimed to evaluate the presence and extent of the association between certain demographic (age and sex) and PD-related (disease duration, cognitive function, anxiety, depression and disability) characteristics and KPPS scores in the Georgian population. To the best of our knowledge, this study represents the first ever scientific application of KPPS in Georgia.

## Materials and methods

**Patient data.** Data collection was performed between November 1, 2023, and May 29, 2024. A total of 100 adult

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*Correspondence to:* Dr Gvantsa Khodeli, School of Medicine, Ilia State University, 3/5 Kakutsa Cholokashvili Avenue, Tbilisi 0179, Georgia  
E-mail: gvantsakhodeli@gmail.com

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patients, aged 45-86 years, were assessed in a single, PD-dedicated facility. Patients outside this age range, patients with Parkinsonism due to drugs or other conditions and those with severe cognitive impairment [Mini Mental State Examination (MMSE) score <20] were excluded. The baseline characteristics of the study sample are presented in Table I.

All patients with a diagnosis of PD who visited The Movement Disorders Referral Centre at the Khechinashvili University Hospital, Tbilisi, Georgia were examined. The present study aimed to assess the correlation between PD-related pain and age, time since disease onset, disability due to impaired mobility, depression severity, anxiety severity, cognitive function and PD severity. Pain was assessed using the KPPS, followed by an objective neurological examination. According to the research protocol for patient assessment, the following tools were also used: The Schwab and England Activities of Daily Living (ADL) scale was used to quantify disability; Beck's Depression Inventory (BDI) (9) was used to evaluate the severity of depression; Generalized Anxiety Disorder Test 7 (GAD-7) (10) was used to measure anxiety severity; Montreal Cognitive Assessment (MoCA) (11) was used to assess the cognitive function of patients; and the Movement Disorder Society-Unified PD Rating Scale (MDS-UPDRS) (12) was used to determine the severity of PD. Self-reported questionnaires, BDI and GAD-7, were completed by the patients on paper in a clinical setting without assistance. MoCA, KPPS, ADL and MDS-UPDRS were administered and scored by the first author.

**Statistical analysis.** Following acquisition, the data were analyzed for associations by biostatisticians (please see the Acknowledgements section below) using SPSS software, version 23.0 (IBM, USA). Pearson's correlation analysis was used for normally distributed data (Kolmogorov-Smirnov normality test,  $P>0.05$ ), while Spearman's Rho was used for non-normally distributed data. KPPS domain 1 data were analyzed using Spearman's Rho due to short scoring scale, while Pearson's correlation was used for other domains and the total score. Correlation coefficients of 0.4-0.69 were considered moderate, while coefficients of 0.1-0.39 were deemed weak. Multiple regression analyses were then performed separately for individual domain and KPPS total scores. In addition, relative risk was calculated between male and female patients for being positive for each item, and individual domain means and KPPS domain and total score means were compared between the sexes. A P-value <0.05 was considered to indicate a statistically significant difference.

## Results

Data analysis revealed moderate, positive correlations between the following variables: GAD score and KPPS total score (Pearson's  $r=0.4$ ,  $P<0.001$ ); MDS-UPDRS and Domain 4 score (Pearson's  $r=0.414$ ,  $P<0.001$ ).

In addition, a weak correlation was present between the following variables: i) GAD score and Domain 1 (Spearman's  $Rho=0.358$ ,  $P<0.001$ ), Domain 3 (Pearson's  $r=0.245$ ,  $P<0.014$ ), Domain 4 (Pearson's  $r=0.359$ ,  $P<0.001$ ), Domain 5 (Pearson's  $r=0.306$ ,  $P=0.002$ ) and Domain 6 scores (Pearson's

Table I. Baseline characteristics of the study population.

Characteristic	No. of participants (n=100)	Percentage
Sex		
Female	58	58.0
Male	42	42.0
Age group (years)		
(mean age, 65.03 years; SD, 10.98 years)		
45-49	9	9.0
50-59	15	15.0
60-69	39	39.0
70-79	30	30.0
80-86	7	7.0
Living arrangements		
With family	87	87.0
Alone	13	13.0
Marital status		
Married	89	89.0
Single	7	7.0
Widowed	4	4.0
Time since disease onset		
(mean, 5.9 years, SD, 4.7 years; range, 0.3-20 years)		
0-4 years	60	60
5-10 years	32	32
11-15 years	7	7
16-20 years	5	5

$r=0.34$ ,  $P<0.001$ ); ii) age and KPPS Domain 3 (Spearman's  $Rho=-0.271$ ,  $P=0.006$ ); iii) Schwab and England ADL score and KPPS Domain 4 (Spearman's  $Rho=-0.247$ ,  $P=0.013$ ) and KPPS total scores (Spearman's  $Rho=-0.233$ ,  $P=0.019$ ); iv) BDI and Domain 1 (Spearman's  $Rho=0.3$ ,  $P=0.002$ ), Domain 4 (Spearman's  $Rho=0.319$ ,  $P=0.001$ ), Domain 5 (Spearman's  $Rho=0.291$ ,  $P=0.003$ ), Domain 7 (Spearman's  $Rho=0.224$ ,  $P=0.025$ ) and KPPS total scores (Spearman's  $Rho=0.313$ ,  $P=0.002$ ); MDS-UPDRS and Domain 1 score (Spearman's  $Rho=0.226$ ,  $P=0.024$ ).

The correlation data between GAD score and KPPS, MDS-UPDRS score and KPPS, and BDI and KPPS are presented in Table II. No statistically significant correlations were found between the length of disease, MoCA score and KPPS total or individual domain scores. Statistically significant correlation scatterplots are presented in Figs. 1-17.

The majority of the correlation data were also reflected in multiple regression models: i) The GAD score was found to be a predictor of Domain 1 ( $P=0.025$ ), Domain 3 ( $P=0.014$ ), Domain 4 ( $P=0.003$ ), Domain 5 ( $P=0.002$ ), Domain 6 ( $P=0.001$ ) and KPPS total scores ( $P<0.001$ ); ii) MDS-UPDRS

Table II. Results of correlation analysis for GAD score and KPPS, MDS-UPDRS score and KPPS and BDI and KPPS.

A, GAD score vs. KPPS domain and total scores

Domain	Pearson's r (Spearman's Rho for Domain 1)	P-value
Domain 1	0.358	<b>&lt;0.001</b>
Domain 2	0.186	0.063
Domain 3	0.245	<b>0.014</b>
Domain 4	0.359	<b>&lt;0.001</b>
Domain 5	0.306	<b>0.002</b>
Domain 6	0.340	<b>&lt;0.001</b>
Domain 7	0.170	0.090
KPPS-total score	0.400	<b>&lt;0.001</b>

B, MDS-UPDRS score vs. KPPS domain and total scores

Domain	Pearson's r (Spearman's Rho for Domain 1)	P-value
Domain 1	0.226	<b>0.024</b>
Domain 2	0.001	0.993
Domain 3	-0.011	0.917
Domain 4	0.414	<b>&lt;0.001</b>
Domain 5	0.131	0.193
Domain 6	0.041	0.683
Domain 7	0.109	0.279
KPPS-total score	0.190	0.059

C, BDI score vs. KPPS domain and total scores

Domain	Spearman's rho	P-value
Domain 1	0.300	<b>0.002</b>
Domain 2	0.027	0.789
Domain 3	-0.029	0.771
Domain 4	0.319	<b>0.001</b>
Domain 5	0.291	<b>0.003</b>
Domain 6	0.039	0.703
Domain 7	0.224	<b>0.025</b>
KPPS-total score	0.313	<b>0.002</b>

Statistically significant correlations ( $P < 0.05$ ) are indicated in bold font. GAD, Generalized Anxiety Disorder Test; KPPS, King's Parkinson's Disease Pain Scale; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; BDI, Beck's Depression Inventory.

score was a predictor of Domain 4 score ( $P < 0.001$ ); iii) Schwab and England ADL predicted-KPPS total score ( $P = 0.044$ ); iv) BDI predicted Domain 1 ( $P < 0.001$ ) (Table III).

No other variables were found to be individual predictors. When comparing men and women, the sex parameter was not found to be a significant risk factor for responding positively to any item (relative risk with  $P \geq 0.1$  for all items, Table IV).

Discussion

The associations between PD-related pain and other clinical and demographic variables have been studied extensively, predating the development of the KPPS. However, due to the weak nature of the correlations, demonstrating their presence has been consistently challenging. For example, previous studies (13-15) have found an association between depression and Parkinsonian pain, while others (16,17) could not report any significant correlation. One possible explanation may be that the studies that found the association had larger sample sizes (314,450,227 vs. 117,96). Although the present study found depression to be correlated with KPPS total and various individual domains by Spearman's correlation analysis, depression was only found to predict a single domain in the multiple regression model, suggesting that even if a weak correlation may exist, a cause-and-effect association between the two is less likely. While the minimal prediction result of the BDI score may be explained by the modest sample size of the present study ( $n = 100$ ), one notable point brought up by in the study by Valkovic *et al* (18) in 2015 paints a more nuanced picture. That study found that, even if average pain intensity is not associated with a higher BDI score, the higher peak pain severity and pain with periodicity are significantly correlated with a higher depression index. This suggested that if, to quantify PD-related pain, one uses different scales that accentuate different facets of pain, the correlations and regression predictions may shift from present to absent, and vice versa.

The association between MDS-UPDRS scores and PD-related pain is also not universally agreed upon. For example, the validation study of KPPS Bulgarian version found an association between MDS-UPDRS part III and KPPS total score (19). However, the full MDS-UPDRS questionnaire was not administered. On the contrary, a Japanese validation study found a correlation with the total MDS-UPDRS score, but not with part III specifically (20). In addition, a study from India demonstrated that the KPPS total correlated with MDS-UPDRS parts II and IV, but not any other parts or the total score (21). In the domain-by-domain regression analysis performed herein, MDS-UPDRS score only predicted KPPS Domain 4; thus, the correlation results in the studies mentioned above may have also been influenced by the frequency of Domain 4 pain in their respective samples (19-21). The clinical significance of this association warrants further assessment in future studies.

If a correlation between depression and PD-related pain is still somewhat debatable, the association between anxiety and PD-related pain has been consistently observed. A Japanese KPPS validation study (20) and two other studies (22,23) have pointed to the presence of the link also observed in the present study.

The consistency of correlations and reflection of all correlations in the regression models in the present

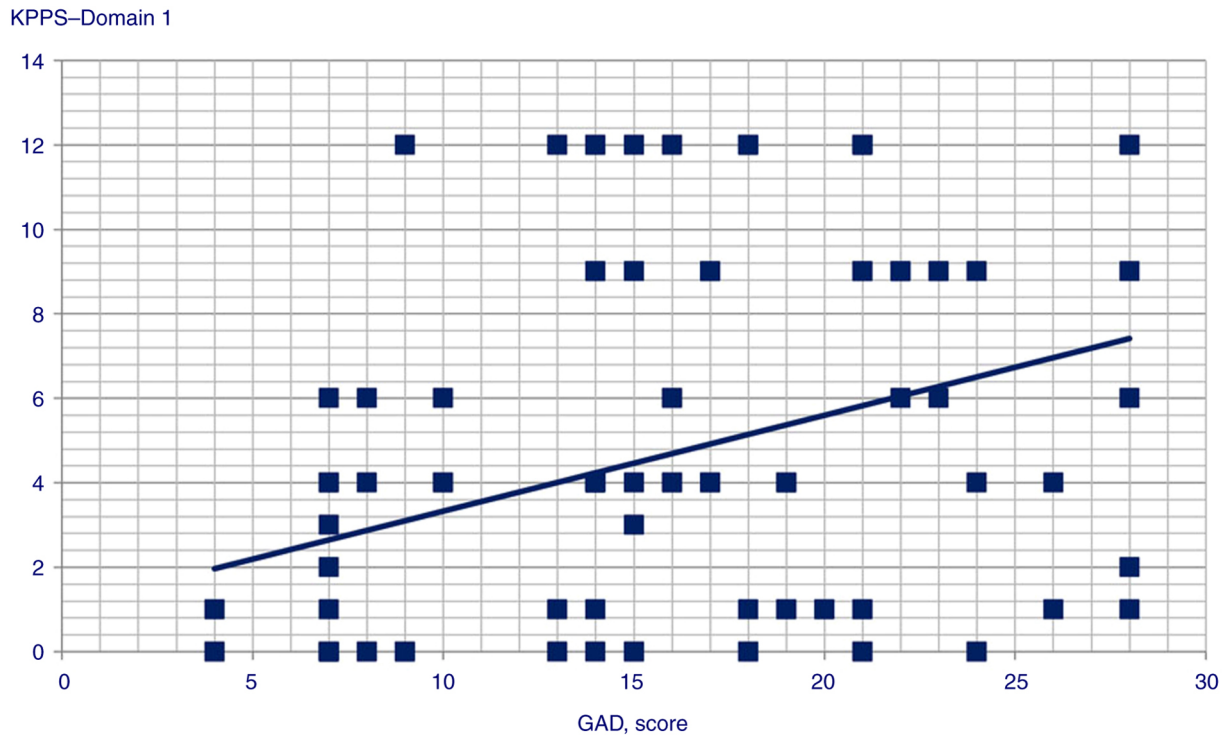


Figure 1. Scatterplot for the correlation between GAD score and KPPS, Domain 1. GAD, Generalized Anxiety Disorder test; KPPS, King's Parkinson's Disease Pain Scale.

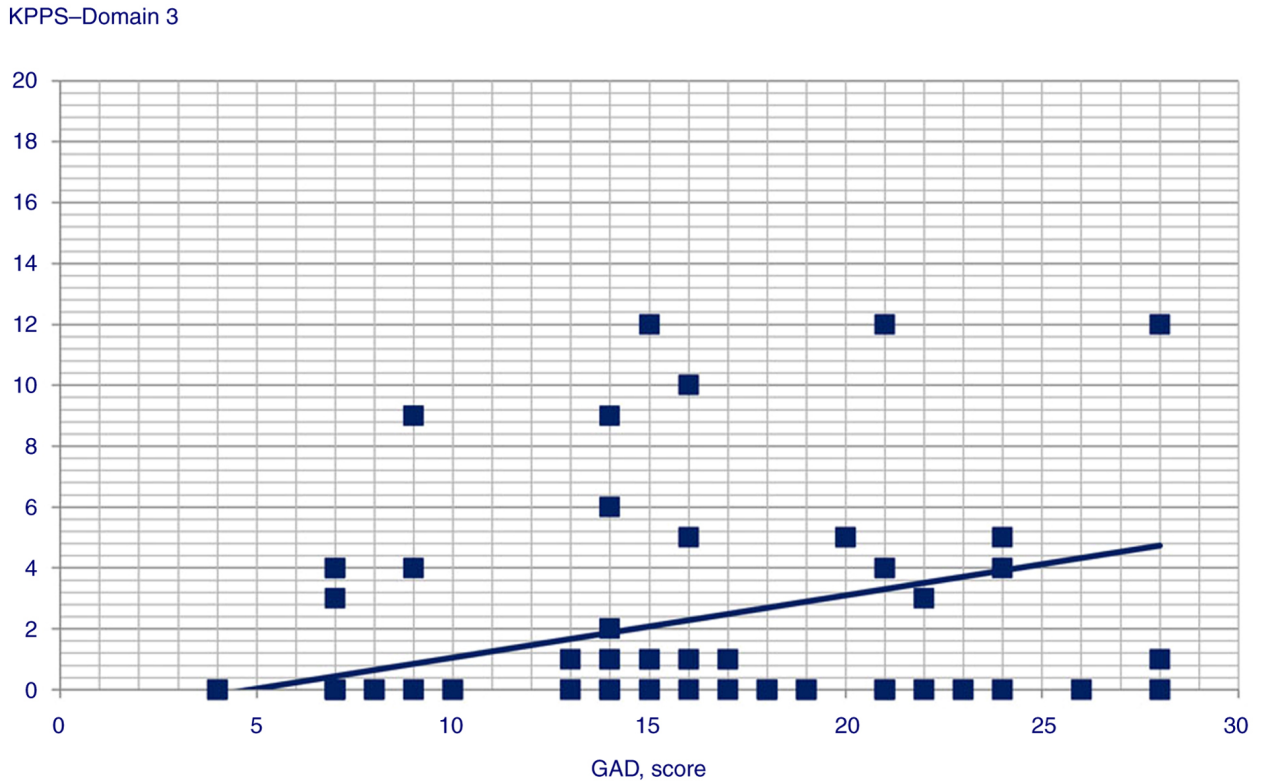


Figure 2. Scatterplot for the correlation between GAD score and KPPS, Domain 3. GAD, Generalized Anxiety Disorder test; KPPS, King's Parkinson's Disease Pain Scale.

study strongly suggested a cause-and-effect association between anxiety and PD-related pain, although causal mechanisms remain to be investigated. The correlation

between pain and lower ADL scores was also consistently shown. In their original study, Chaudhuri *et al* (8) used the Scales for Outcomes in Parkinson's disease-Motor

KPPS–Domain 4

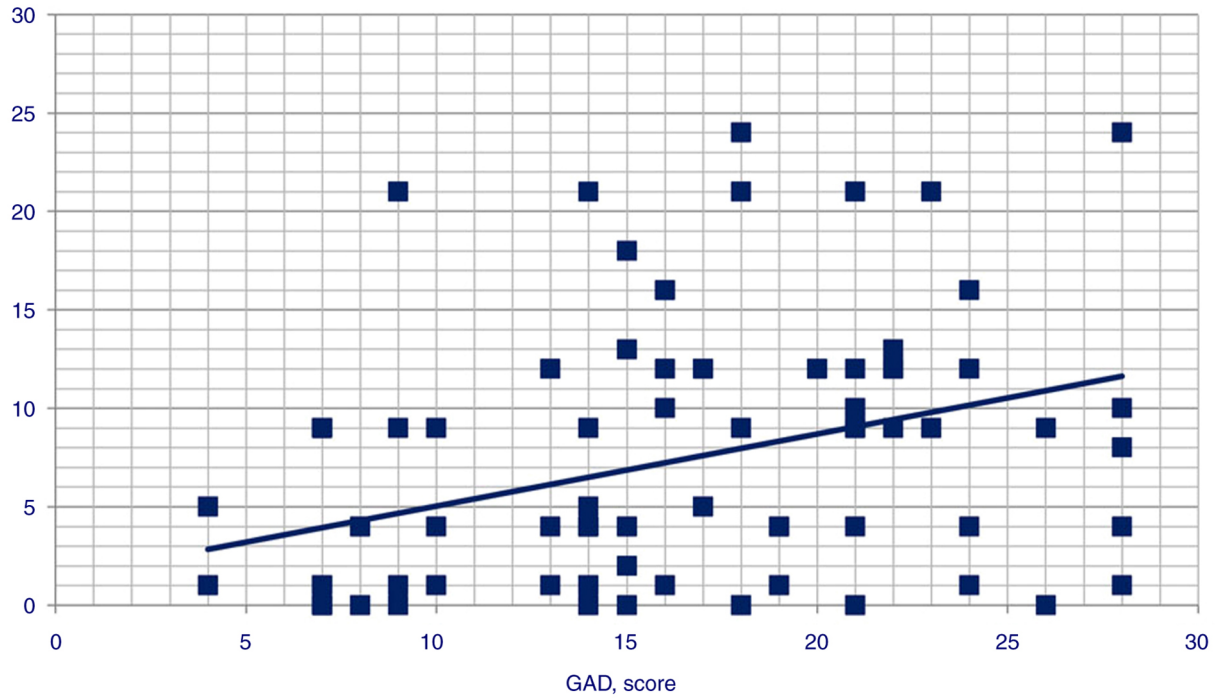


Figure 3. Scatterplot for the correlation between GAD score and KPPS, Domain 4. GAD, Generalized Anxiety Disorder test; KPPS, King's Parkinson's Disease Pain Scale.

KPPS–Domain 5

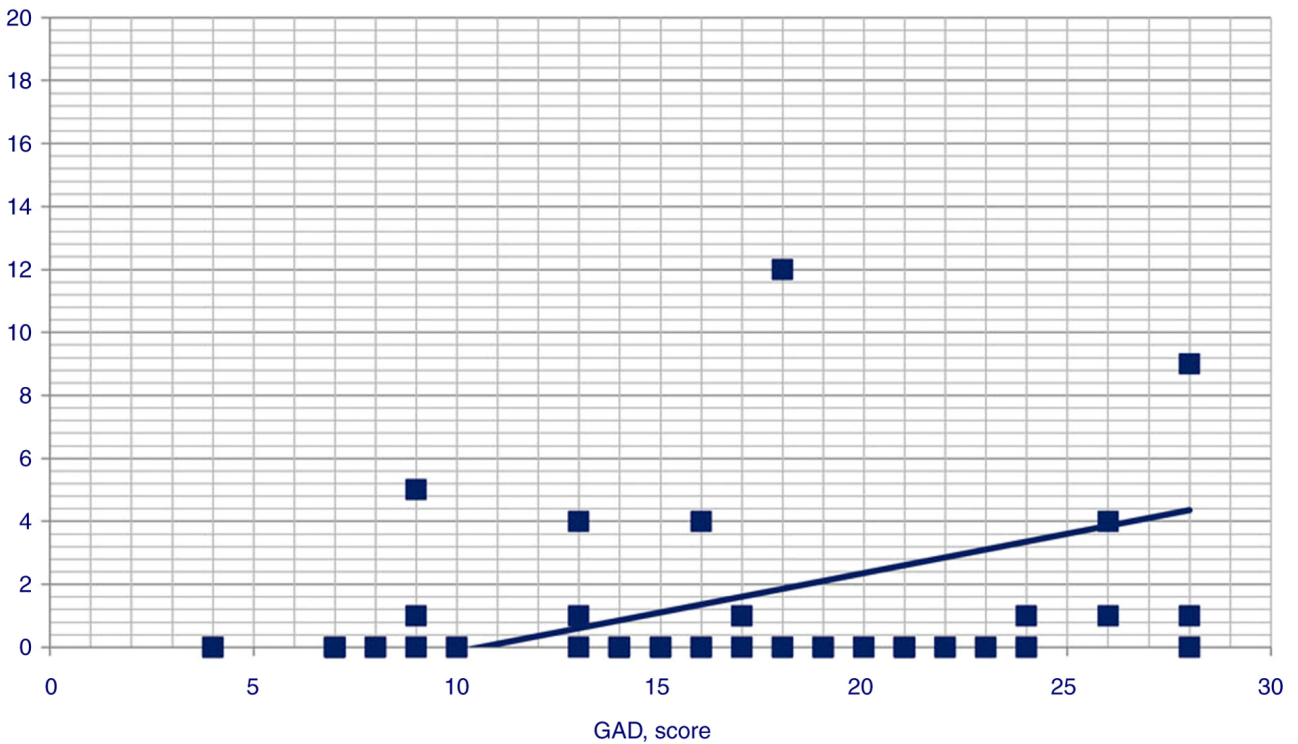


Figure 4. Scatterplot for the correlation between GAD score and KPPS, Domain 5. GAD, Generalized Anxiety Disorder test; KPPS, King's Parkinson's Disease Pain Scale.

ADL (SCOPA-Motor ADL) score, while a Chinese validation study (22), as in the present study, used Schwab and

England ADL score, with moderate correlations found in both instances.

KPPS–Domain 6

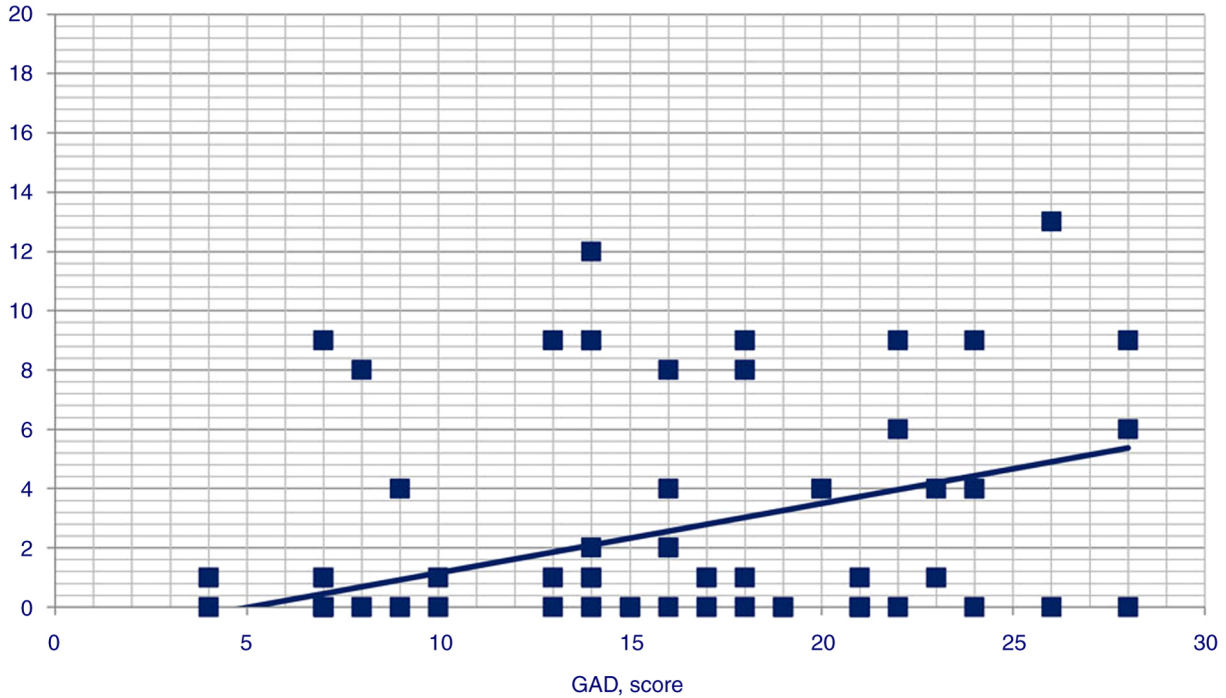


Figure 5. Scatterplot for the correlation between GAD score and KPPS, Domain 6. GAD, Generalized Anxiety Disorder test; KPPS, King's Parkinson's Disease Pain Scale.

KPPS–Total

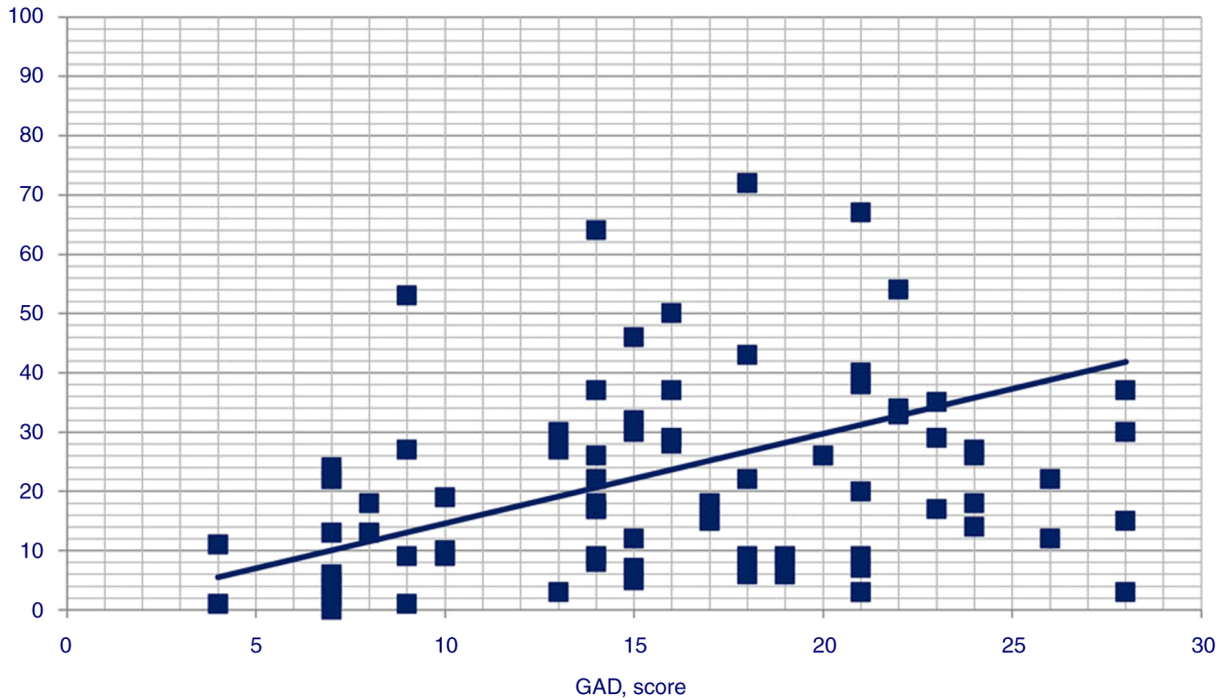


Figure 6. Scatterplot for the correlation between GAD score and KPPS total score. GAD, Generalized Anxiety Disorder test; KPPS, King's Parkinson's Disease Pain Scale.

Although the present study further confirmed the absence of an association between the age of the patients and KPPS total score, consistent with previous studies (8,13,22), a weak association was noted for age and musculoskeletal

pain (Domain 1). This correlation was likely at least partially confounded, considering that 58% of the present sample were female; female patients are at a higher risk of developing osteoporosis and the prevalence of osteoporosis

KPPS–Domain 4

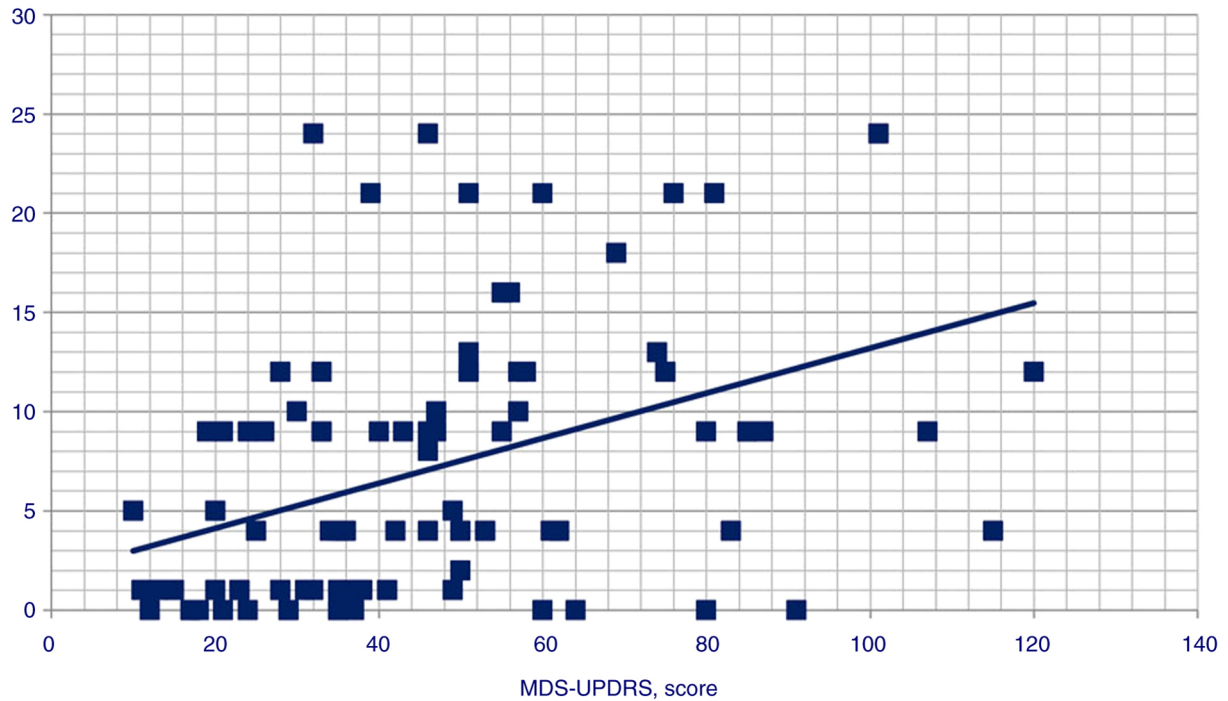


Figure 7. Scatterplot for the correlation between MDS-UPDRS score and KPPS, Domain 4. MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; KPPS, King's Parkinson's Disease Pain Scale.

KPPS–Total

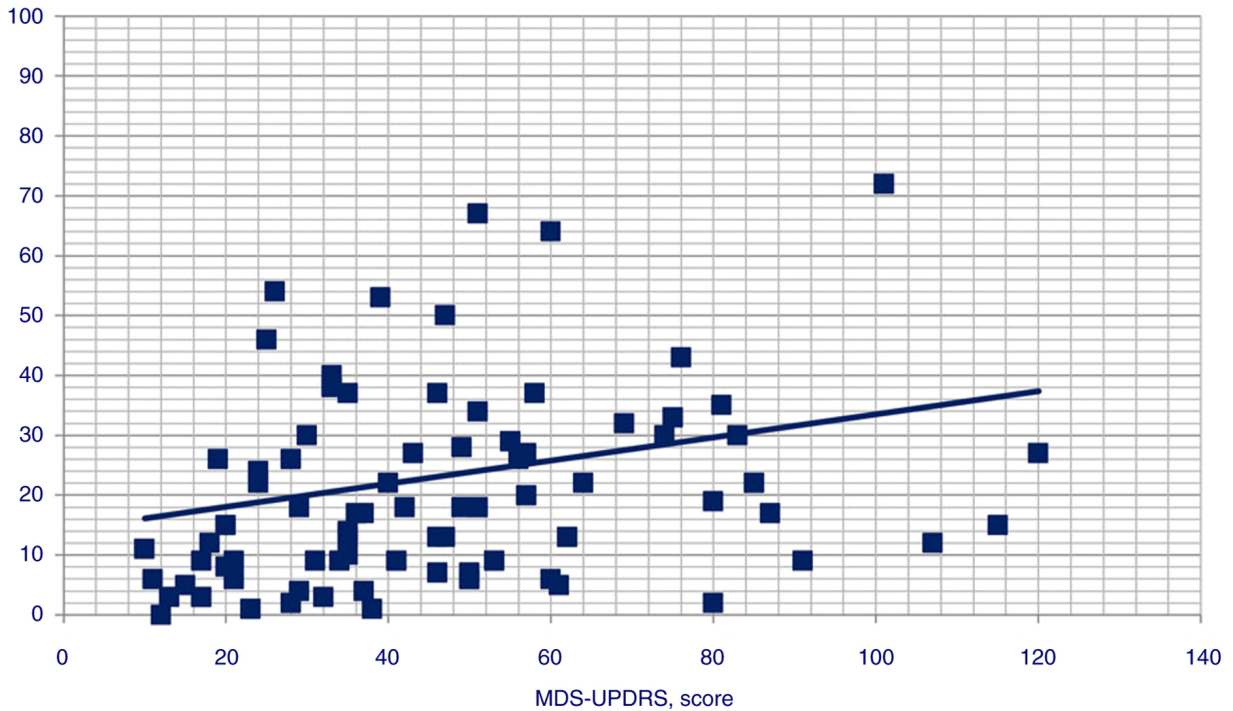


Figure 8. Scatterplot for the correlation between MDS-UPDRS score and KPPS total score. MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; KPPS, King's Parkinson's Disease Pain Scale.

increases with age (24). However, as osteoporosis data were not collected in the present study, this remains speculative.

Disease duration has been cited as the variable correlated with KPPS scores (8,20). However, the Chinese validation study resulted in the correlation being just



KPPS–Total

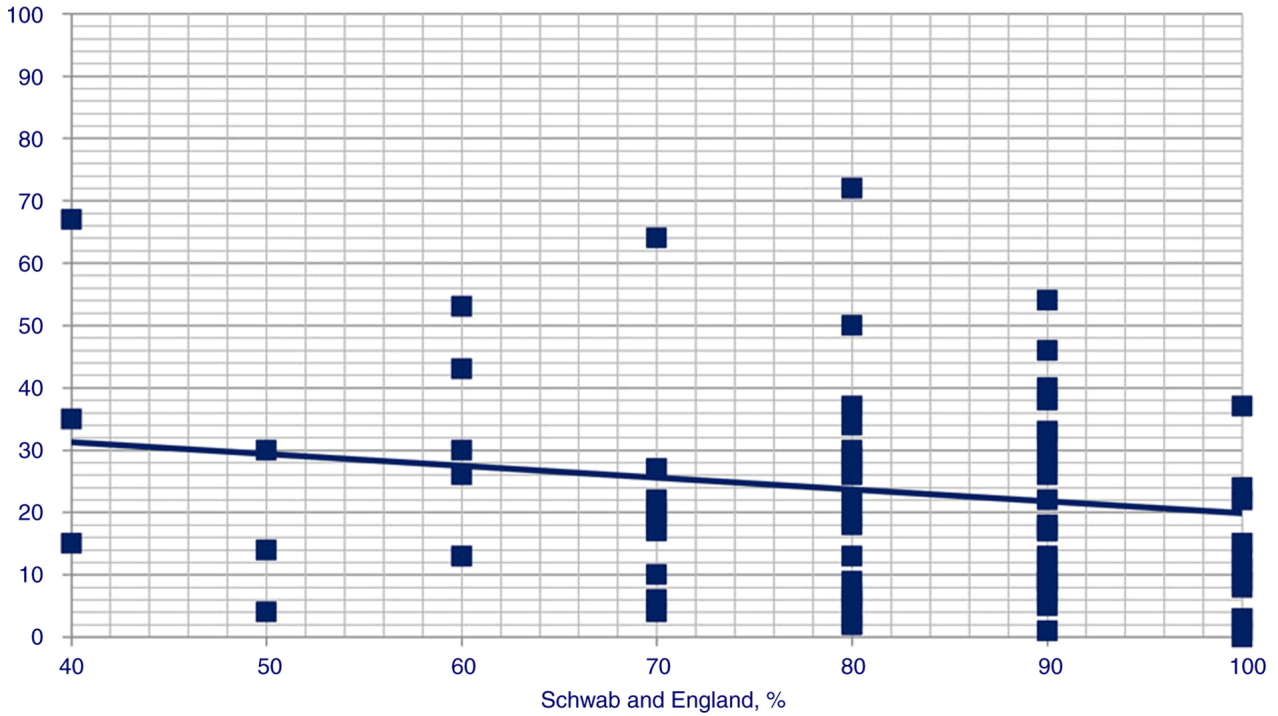


Figure 11. Scatterplot for the correlation between Schwab and England score and KPPS total score. KPPS, King's Parkinson's Disease Pain Scale.

KPPS–Domain 1

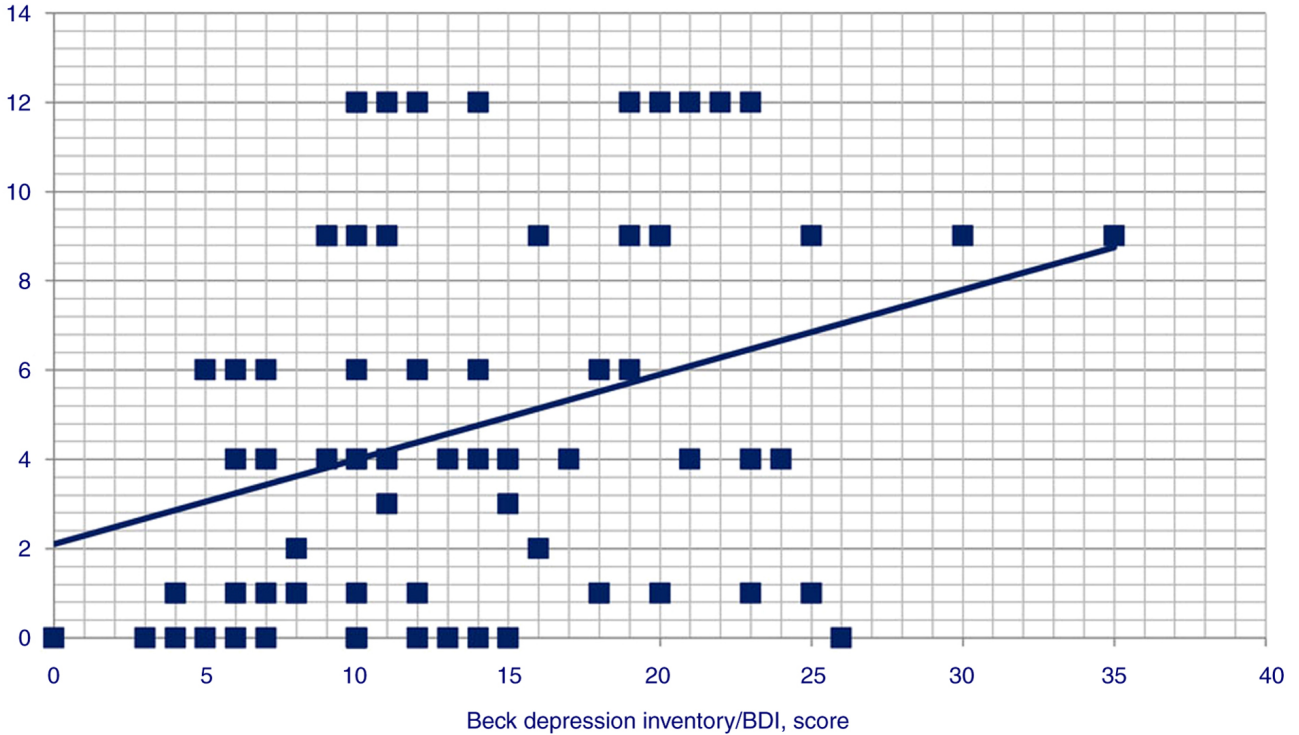


Figure 12. Scatterplot for the correlation between BDI and KPPS, Domain 1. BDI, Beck Depression Index; KPPS, King's Parkinson's Disease Pain Scale.

Findings in previous studies are rather inconsistent regarding sex. While certain studies have found a link between female sex and higher KPPS scores (21,25), others

did not (8,22). The present study found no significant sex-based differences in PD-related pain. A similar disagreement in sex-based differences in pain was found in studies

KPPS–Domain 4

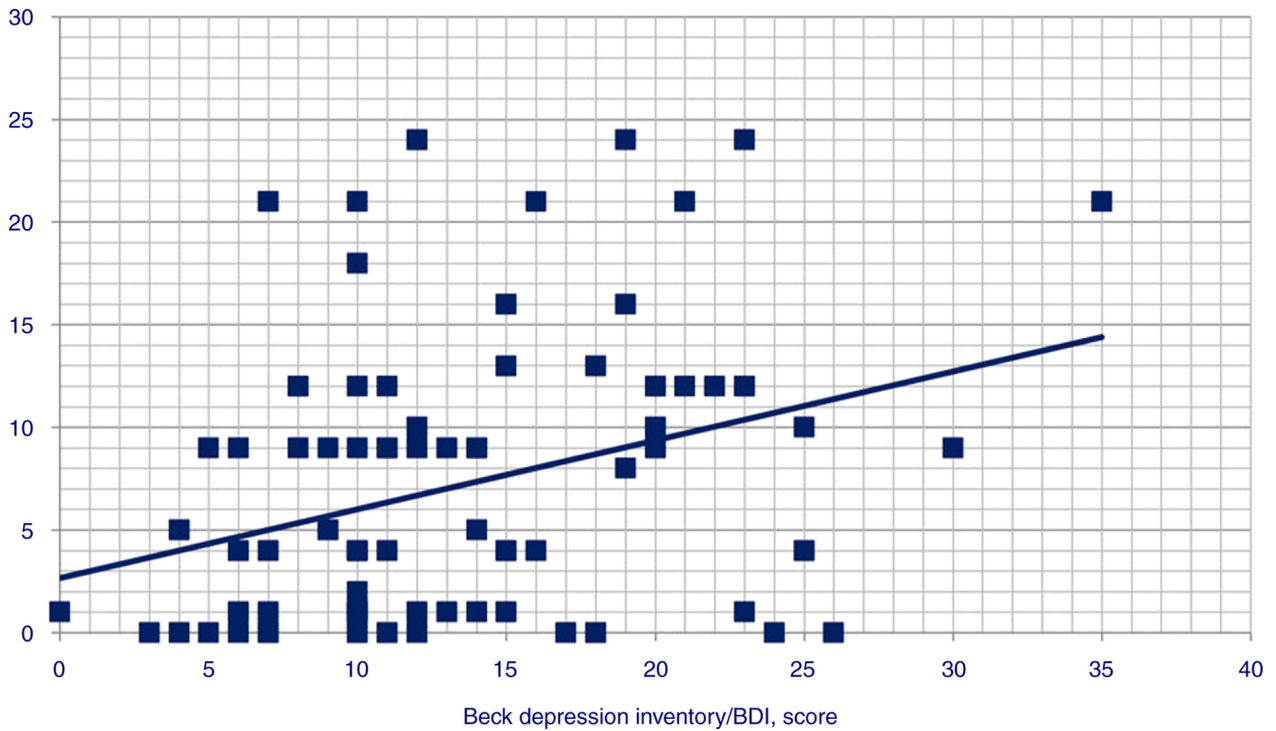


Figure 13. Scatterplot for the correlation between BDI and KPPS, Domain 4. BDI, Beck Depression Index; KPPS, King's Parkinson's Disease Pain Scale.

KPPS–Domain 5

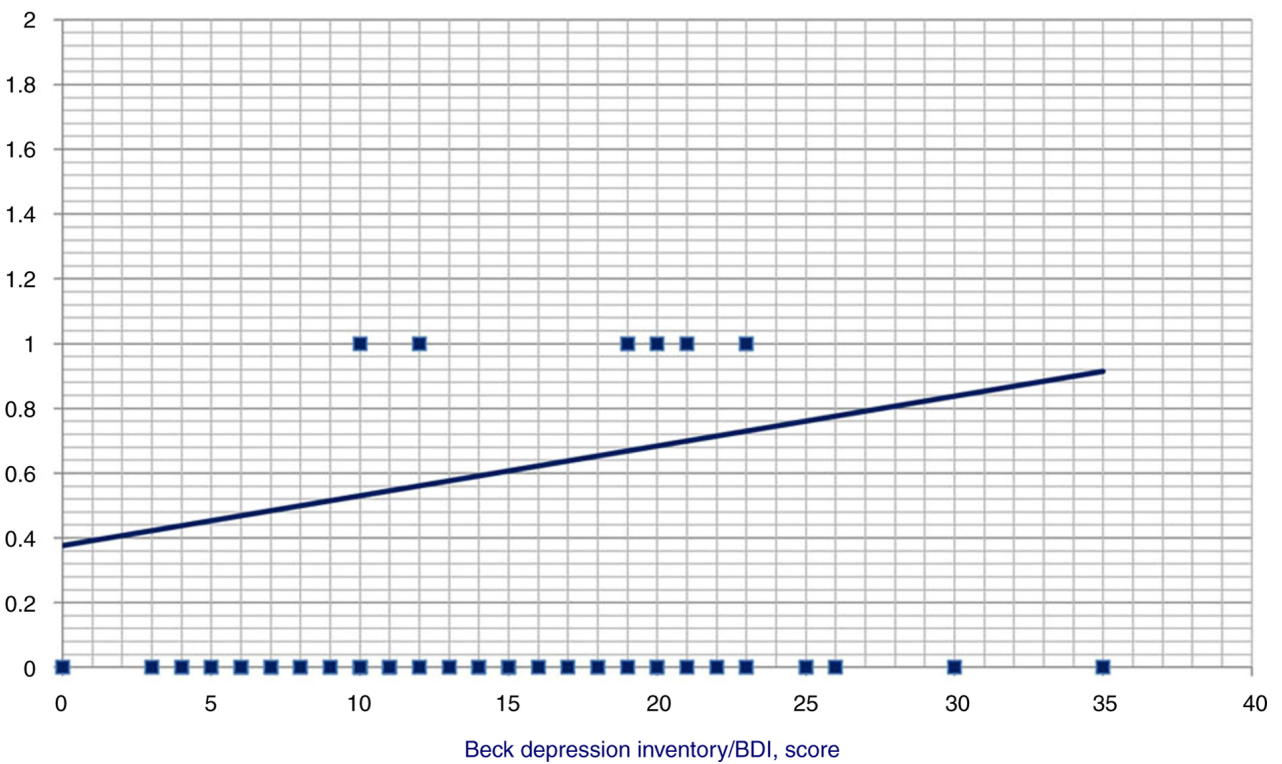


Figure 14. Scatterplot for the correlation between BDI and KPPS, Domain 5. BDI, Beck Depression Index; KPPS, King's Parkinson's Disease Pain Scale.

that did not use KPPS (26,27). In the present study, sex was not found to be a risk factor for item positivity or higher

domain scores. This discrepancy suggested that sex-based differences in PD-related pain warrant further exploration.

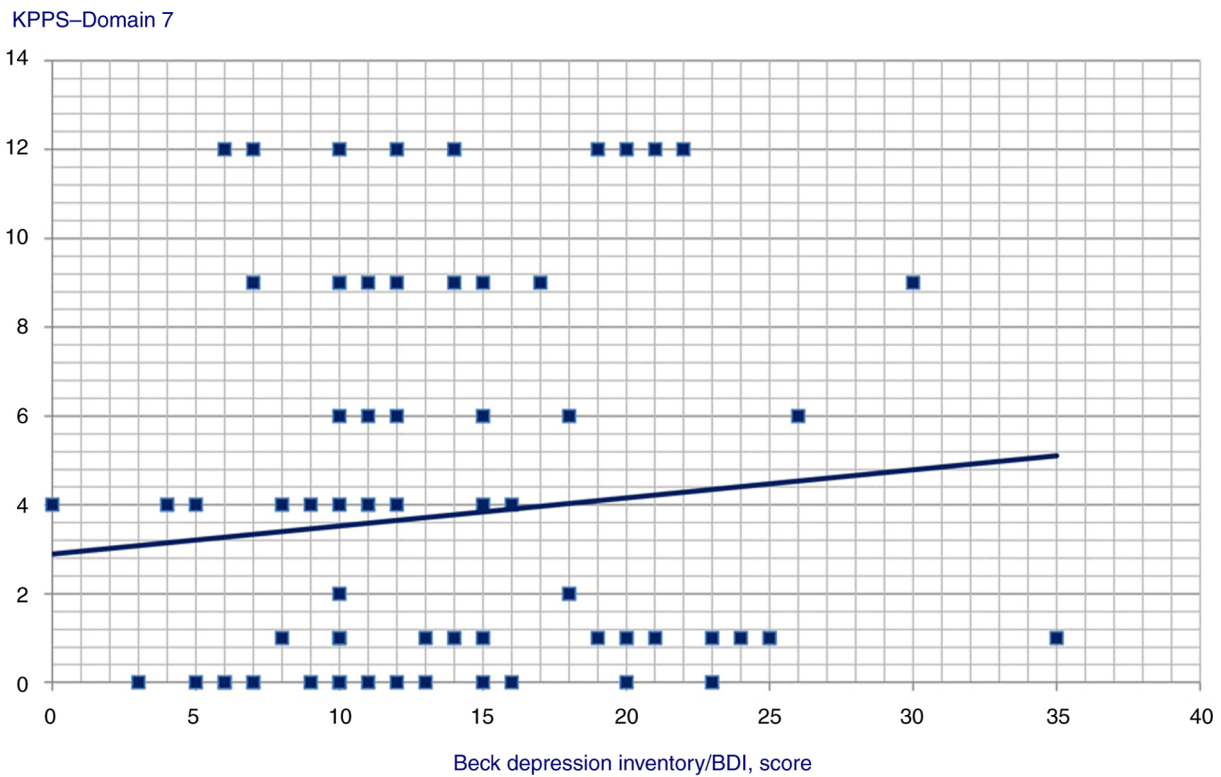


Figure 15. Scatterplot for the correlation between BDI and KPPS, Domain 7. BDI, Beck Depression Index; KPPS, King's Parkinson's Disease Pain Scale.

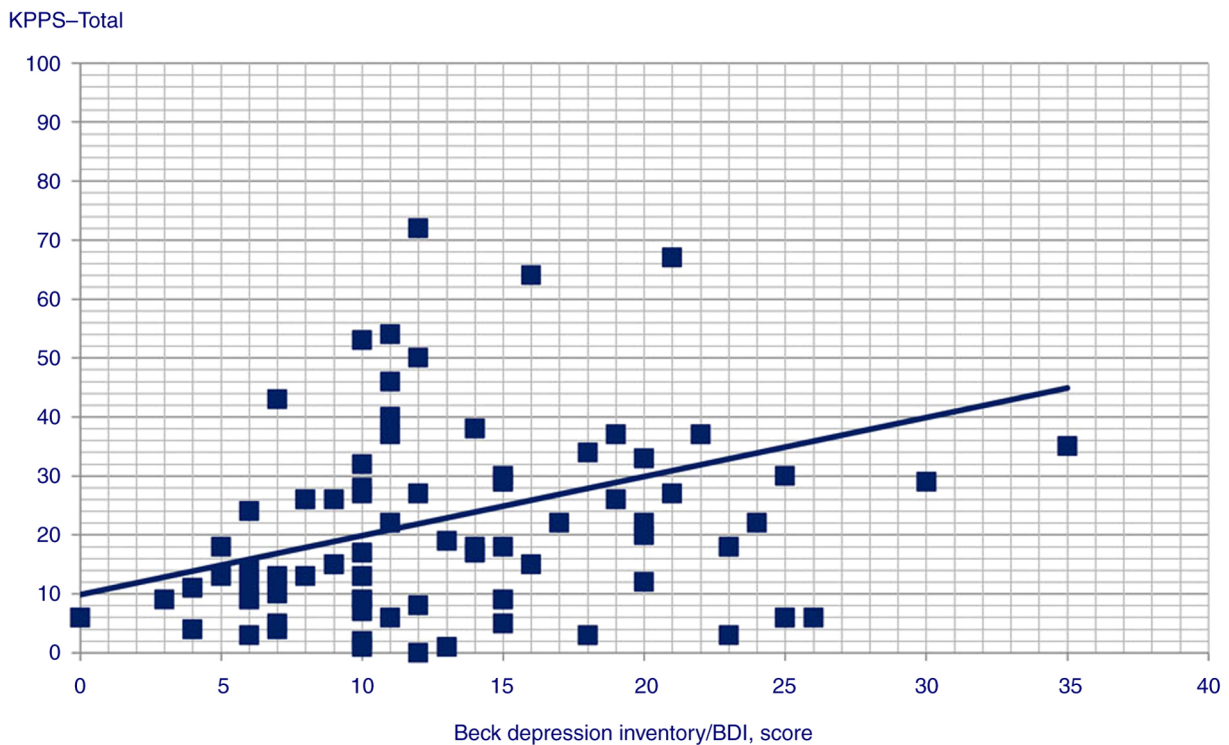


Figure 16. Scatterplot for the correlation between BDI and KPPS total score. BDI, Beck Depression Index; KPPS, King's Parkinson's Disease Pain Scale.

MoCA and KPPS total score correlation analysis were not performed in any previous study; however, previous studies that touched on the topic of PD-related pain and cognitive decline reported no such association (28,29). These results were consistent with prior findings.

Considering the above, there is a need for further research regarding the association between clinical and demographic variables and PD-related pain. The majority of studies on the subject are performed in distinct, country-specific populations. The present study added Georgia to the geographic areas

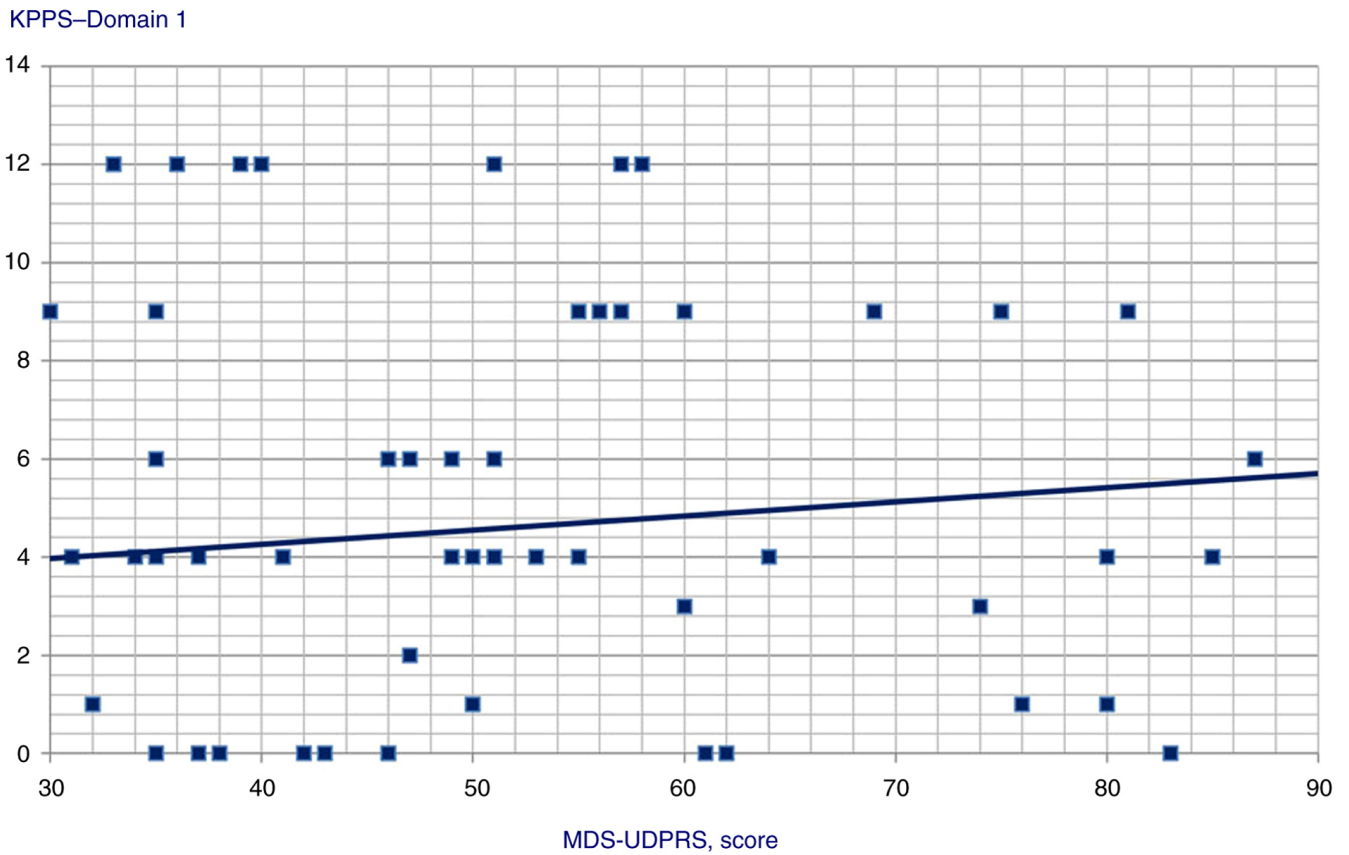


Figure 17. Scatterplot for the correlation between MDS-UPDRS score and KPPS, Domain 1. MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; KPPS, King's Parkinson's Disease Pain Scale.

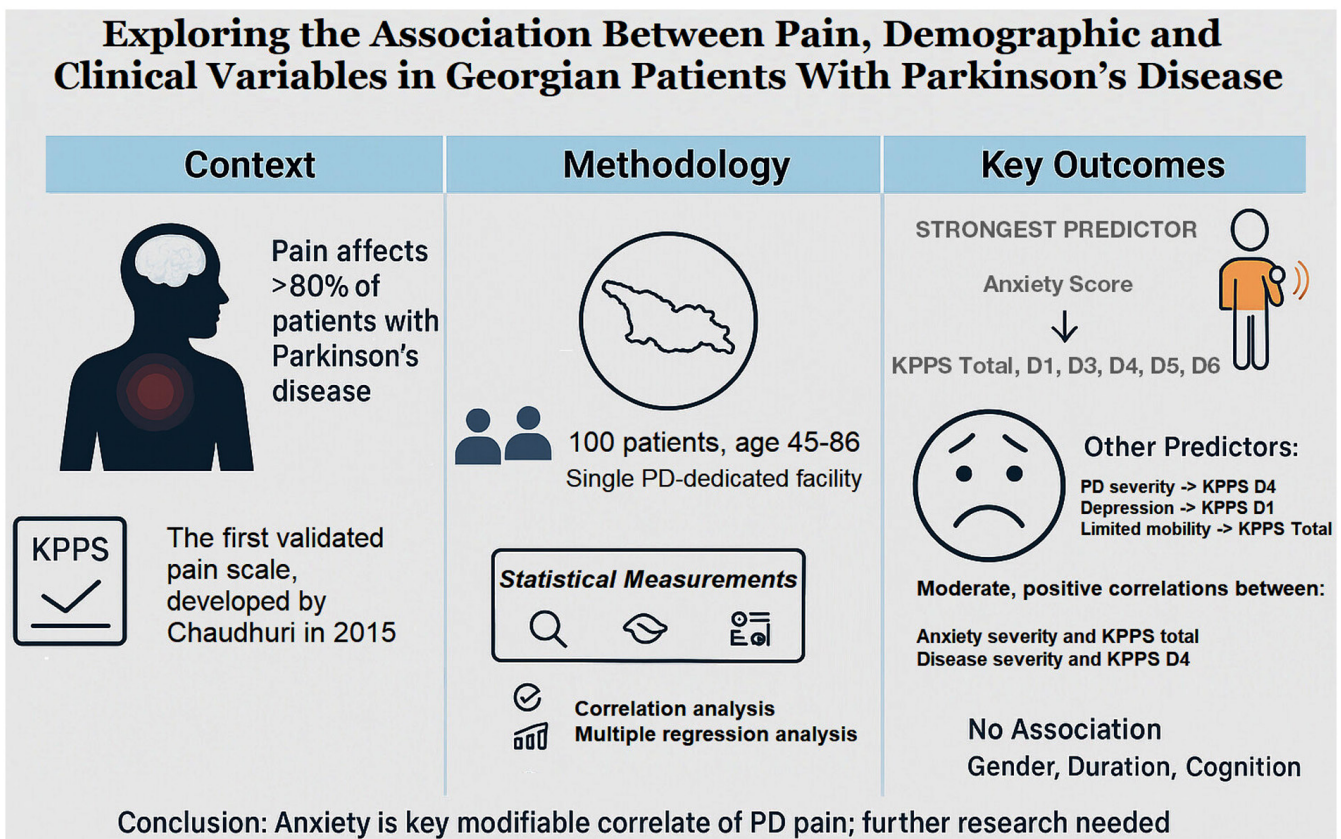


Figure 18. Graphical image summarizing the findings of the present study.

Table III. Statistically significant predictors from multiple regression analysis models.

Outcome variable	Predictor	Statistics
KPPS total score	Schwab and England score	Beta coefficient=-0.08; t=2.05, P=0.044
	GAD score	Beta coefficient=0.39; t=4.17, P<0.001
KPPS, Domain 1	BDI score	Beta coefficient=0.10; t=3.82, P<0.001
	GAD score	Beta coefficient=0.28; t=2.28, P=0.025
KPPS, Domain 2	GAD score	Beta coefficient=0.28; t=2.28, P=0.025
KPPS, Domain 3	GAD score	Beta coefficient=0.25; t=2.50, P=0.014
KPPS, Domain 4	GAD score	Beta coefficient=0.28; t=3.06, P=0.003
	MDS-UPDRS score	Beta coefficient=0.35; t=3.86, P<0.001
KPPS, Domain 5	GAD score	Beta coefficient=0.31; t=3.18, P=0.002
KPPS, Domain 6	GAD score	Beta coefficient=0.34; t=3.58, P=0.001

KPPS, King's Parkinson's Disease Pain Scale; GAD, Generalized Anxiety Disorder Test; BDI, Beck's Depression Inventory; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale.

Table IV. Proportion of patients with positive responses of KPPS (n=100) by sex.

Items	Females		Males		RR (95% CI)	P-value
	No. of patients	%	No. of patients	%		
Musculoskeletal pain	47	81.0	29	69.0	1.35 (0.84-2.16)	0.211
Pain deep within the body	8	13.8	7	16.7	0.91 (0.55-1.50)	0.704
Pain related to an internal organ (e.g. pain in the liver, stomach or intestines-visceral pain)	3	5.2	4	9.5	0.72 (0.30-1.73)	0.469
Dyskinetic pain	7	12.1	6	14.3	0.91 (0.54-1.57)	0.755
'Off' period dystonia in a specific area	10	17.2	9	21.4	0.88 (0.56-1.41)	0.616
Generalized 'off' period pain	4	6.9	7	16.7	0.60 (0.27-1.33)	0.209
Pain associated with periodic limb movements (PLM) or an unpleasant burning sensation in the legs that improves with movement	24	41.4	11	26.2	1.31 (0.95-1.81)	0.100
Pain associated with difficulty turning over in bed at night	43	74.1	31	73.8	1.01 (0.69-1.48)	0.971
Pain when chewing	6	10.3	5	11.9	0.93 (0.53-1.65)	0.812
Pain due to grinding teeth in sleeping	0	0.0	0	0.0	N/A	N/A
Burning mouth syndrome	3	5.2	2	4.8	1.03 (0.50-2.16)	0.924
Burning pain in limbs	26	44.8	17	40.5	1.08 (0.77-1.50)	0.663
Generalized lower abdominal pain	4	6.9	4	9.5	0.85 (0.42-1.74)	0.660
Sharp/stabbing pain in the lower limbs	43	74.1	29	69.0	1.11 (0.75-1.65)	0.588

RR, relative risk; CI, confidence interval; N/A, not applicable.

covered, and to the best of our knowledge, correlations with individual KPPS domains were explored herein for the first time.

The adjustment for the results of multiple regression analyses and correlations was not performed in the present study, introducing a theoretical risk of type I error. However, since

the link between anxiety and KPPS domains, which was the main finding of the present study, was consistent with multiple previous studies (20,22,23), this possibility is deemed unlikely. Still, the predictive connection between MDS-UPDRS and KPPS Domain 4 score may be potentially impacted, and this lack of adjustment (by Bonferroni, Sidak or other methods) can be considered as a limitation of the present study.

In conclusion, the present study found that higher GAD scores were correlated with and could predict KPPS Domains 1, 3, 4, 5 and 6, and KPPS total scores, supporting the hypothesis of a potential causal association, consistent with prior evidence. The MDS-UPDRS score correlated with and predicted the KPPS Domain 4 score. The association between depression and pain may be subtle and nuanced, although a direct causal link is less likely. The positive correlation between BDI score and musculoskeletal pain in the present study is probably confounded. No association was found between KPPS and disease duration, MoCA score or sex. Future studies with larger, more diverse samples are required to confirm these findings and explore additional contributing factors. The findings of the present study are summarized in the diagram illustrated in Fig. 18.

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### Availability of data and materials

The data generated in the present study are available from the corresponding author on reasonable request.

### Authors' contributions

GK wrote the first draft of the manuscript and ensured its submission to the journal. All authors (GK, AT, MG, SS, IK and MM) contributed to the conception and design of the study, material preparation, data collection, analysis and interpretation. AT contributed to the analysis of the data and draft editing. SS, IK and MM revised the manuscript critically for important intellectual content. All authors have read and

approved the final version of the article. GK and AT confirm the authenticity of all the raw data.

### Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Ilia State University (approval no. R/244-23 Tbilisi, Georgia). The study was conducted with the voluntary written consent of the participants or their guardians. Research subjects could withdraw from the study at any stage and all information obtained was used solely for research purposes.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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