# Prevalence and duration of non-motor symptoms in prodromal Parkinson's Disease

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# Prevalence and duration of non-motor symptoms in prodromal Parkinson's Disease

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**Abstract**

**Background:** The prevalence and duration of NMS in prodromal PD has not been extensively studied. The aim of this study was to determine the prevalence and duration of prodromal NMS (pNMS) in a cohort of recently diagnosed PD patients.

**Methods:** We evaluated the prevalence and duration of prodromal NMS in early PD patients (n= 154). NMS were screened for using the Nonmotor Symptom Questionnaire (NMS Quest). We subtracted the duration of the presence of each individual NMS reported from the duration of earliest motor symptom. NMS whose duration preceded the duration of motor symptoms were considered a pNMS. Individual pNMS were then grouped into relevant pNMS clusters based on the NMSQuest domains.

Motor subtypes were defined as tremor dominant (TD), postural instability/gait difficulty (PIGD) and indeterminate type according to the MDS-UPDRS revision.

**Results:** pNMS were experienced by 90.3% of PD patients and the median number experienced were 4 (IQR: 2 -7). A gender difference in pNMS experienced existed, with males reporting more sexual dysfunction, forgetfulness, dream re-enactment. Conversely, females reported more unexplained weight change and anxiety.

There was a significant association between any prodromal gastrointestinal symptoms (OR=2.30, 95% CI=1.08-4.89, P=0.03) and urinary symptoms (OR=2.54, 95% CI=1.19-5.35,

p=0.016) with the PIGD phenotype. Further analysis revealed that total pNMS was not significantly associated with having PIGD phenotype (OR= 1.105, 95% CI=0.99-1.21, p=0.068).

**Conclusion:** pNMS are common and a gender difference in pNMS experienced in prodromal PD may exist. PIGD phenotype had a higher prevalence of prodromal gastrointestinal and urinary tract symptoms.

## Introduction

Clinically, PD has been defined by the presence of motor deficits such as bradykinesia, tremor, rigidity and postural instability [1]. However, PD patients also experience a variety of other non-motor symptoms (NMS) such as mood disorders, autonomic disturbances, cognitive impairment and sleep dysfunction throughout their disease trajectory.

NMS can precede motor symptoms indicating a prodromal symptomatic stage exists in PD. The presence of hyposmia, constipation, depression and idiopathic REM (rapid eye movement) Sleep Behaviour Disorder (RBD) are well-established symptoms that significantly increase the risk of development of PD [2].

The emerging concept of a prodromal phase of PD has led the International Parkinson and Movement Disorder Society (IPMDS) task force to propose a new definition of PD; this definition would not base the diagnosis solely on motor symptoms but would also incorporate NMS [3]. However, there is a paucity of research investigating the frequency and time of onset of NMS before the onset of the motor phase of PD. Furthermore, little is known about the relationship between particular clusters of prodromal NMS and the development of

subsequent PD motor phenotypes: tremor dominant (TD), postural instability gait difficulty (PIGD) types or indeterminate type [4].

We aimed to explore the frequency and time of onset of NMS before motor symptoms (prodromal NMS, pNMS) and the role of gender on pNMS experienced. We hypothesised that distinct clusters of pNMS would be associated with PIGD motor phenotype.

## Methods

### Patient eligibility criteria and recruitment

Recently diagnosed PD patients from Newcastle-upon-Tyne and Gateshead were invited to take part in the study between June 2009, and December 2011 as part of the Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation-Parkinson's disease (ICICLE-PD) study [5].

All participants were diagnosed by a movement disorders specialist according to the UK Brain Bank criteria [1]. Exclusion criteria comprised the following: drug-induced parkinsonism secondary to exposure to dopamine receptor blocking agent at the onset of symptoms; vascular parkinsonism; and atypical forms of parkinsonism such as progressive supranuclear palsy, multiple system atrophy, or corticobasal degeneration, according to accepted diagnostic criteria [6]. Participants were also excluded if they had insufficient working knowledge of English, defined as being unable to perform the assessments and questionnaires in the opinion of the assessor, or significant memory impairment or dementia at presentation,

defined a Mini-Mental State Examination (MMSE) score <24, fulfilling DSM-IV criteria for dementia [7] or Movement Disorder Society (MDS) criteria for PDD [8].

The study was approved by the Newcastle and North Tyneside Research Ethics Committee and performed according to the Declaration of Helsinki. All participants provided informed written consent.

**Assessments**

PD participants were rated for disease severity by Hoehn & Yahr staging and motor severity using the MDS Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III. Motor subtypes were defined as TD, PIGD and indeterminate type according to the methods described by Jankovic et al [9]. Due to the small numbers of indeterminate motor phenotype in the cohort, only comparisons between motor subtype of TD and PIGD were conducted. Levodopa equivalent daily dose (LEDD) was calculated for all dopaminergic medications using methods described by Tomlinson et al [10].

Global cognition was assessed using the MMSE and the Montreal Cognitive Assessment (MoCA). Depressive symptoms were also assessed using the Geriatric Depression Scale (GDS-15).

**Assessment of NMS and prodromal NMS.**

Participant NMS burden was assessed at initial patient screening visit using the Non-Motor Symptom Questionnaire (NMS-Quest) [11] . The NMS-Quest is 30-item questionnaire, which comprises ten domains of NMS: gastrointestinal symptoms, urinary tract symptoms, sexual function, cardiovascular issues, depression/anxiety, sleep problems/fatigue, pain and number

of other complaints such as weight loss. A positive response about the presence of a NMS on the screening questionnaire, elicited a further question about the estimated duration of the NMS symptom.

In order to determine the presence or absence of pNMS, we subtracted the duration of the presence of each individual NMS reported from the duration of earliest motor symptom. NMS whose duration preceded the duration of motor symptoms were considered a pNMS; NMS which occurred after motor symptom onset were not classified as pNMS. The presence and duration of each NMS in excess of the duration of motor symptoms was recorded as a pNMS in months.

Individual pNMS symptoms were further classified into seven distinct non-motor subtypes based on the symptom domains covered in the NMS-Quest. These were gastrointestinal symptoms, urinary tract symptoms, sexual dysfunction, cardiovascular symptoms, neuropsychiatric and cognitive symptoms, sleep dysfunction symptoms and miscellaneous symptoms. In order to be included in a prodromal non-motor subtype, a participant had to have at least one prodromal NMS consistent with that NMS domain.

**Statistical analysis**

Statistical analyses were performed using SPSS software (Version 22, Armonk, NY: IBM Corp). Data were assessed for a normality using Kolmogorov-Smirnov tests. The mean and standard deviation were computed for parametric variables, the median and interquartile range for non-parametric variables. Continuous and count data were compared using the parametric tests (T- test) or non-parametric test (Mann Whitney U) as appropriate, and categorical data with $\chi 2$ tests.

Hierarchical logistic regression was used to determine significant predictors of PIGD motor phenotype. Backwards stepwise logistic regression was used to produce a basic model of predictors involving age, gender and LEDD. Non-significant predictors were excluded. Significant predictors were then included to give a basic model; total pNMS and pNMS domains (present or absent) were then individually added to the model. A p-value of <0.05 was deemed to be significant for all analysis.

**Results**

154 participants with a diagnosis of idiopathic PD were identified from the ICICLE-PD cohort (Table 1). Participants had a mean age of 66.4±10.4 years and had a median PD duration of 4.7 months; 64.9% (n=100) were male.

The presence or absence of pNMS was calculated; 139 (90.3%) of participants experienced pNMS (Table 2). The median number of pNMS experienced by the PD patients was 4 (IQR: 2 -7). The most common individual pNMS experienced were: hyposmia (39.6%); forgetfulness/memory complaints (36%); sialorrhea (33.8%); urinary urgency (30.2%); and anxiety (30.2%) (Table 2). Gender differences in pNMS experienced were observed, with males reported significantly more sexual dysfunction (22% vs 3.7%, respectively, p=0.003), forgetfulness (38% vs 22.2%, respectively, p=0.046), dream re-enactment (29% vs 14.8%, respectively, p=0.049) compared to female participants (Table 2). Conversely, females reported significantly greater unexplained weight change (13% vs 4%, respectively, p=0.039) and anxiety (37% vs 22%, respectively, p=0.046).

Individual pNMS symptoms were classified into prodromal NMS domains. The most frequent pNMS domains were gastrointestinal tract (67.5%), sleep (52.6%), urinary tract (42.2%), cardiovascular system (32.5%) and miscellaneous systems (22.1%) (Table 3). In terms of the median duration of pNMS preceding motor symptom onset, sleep dysfunction (-66 months), sexual dysfunction (-60 months) and gastrointestinal tract symptoms (-59months) had the longest latency period (Table 3).When pNMS were grouped into symptom clusters, males experienced significantly more symptoms related to sexual problems compared to female participants (26% vs 5.6%, respectively, p=0.002, Table 3); females experienced significantly more miscellaneous symptoms compared to male participants (40.7% vs 19%, respectively, p=0.004).

Prodromal NMS differences between motor phenotypes were then evaluated (Table 4). Participants classified as PIGD were significantly older than TD subtypes (68.4±9.2 vs. 63.6±11), respectively, p=<0.01; Table 4). The Geriatric Depression Scale (GDS-15) scores were slightly higher for the PIGD subtype compared to the TD subtype (3.12±2.4 vs. 2.27 ± 2.3, respectively, p=0.01), but were still below the cut-off (≥5) for possible depression in all subtypes. Participants with PIGD subtype were prescribed significantly higher doses of LEDD compared with TD subtype (203.0 ± 138.6 vs 151.4 ±165.4, respectively, p<0.01) (Table 4).

Predictors of PIGD motor phenotype were then determined, first using logistic univariate regression. Significant predictors included age, LEDD, GDS-15, number of pNMS, gastrointestinal symptoms and urinary symptoms (Table 4).

Backwards regression revealed that only age (β=0.061, OR=1.06, CI=1.02-1.11, p=0.003) was a significant predictor of PIGD phenotype; a basic model was then constructed with age and LEDD. LEDD was included in the basic model as it was an important confounding variable although it was not a significant predictor of PIGD phenotype. Total pNMS and pNMS domains were then individually added to the model. Analysis revealed that total pNMS was not a significant predictor of having PIGD phenotype (OR= 1.10, CI=0.99-1.21 p>0.05). However, there was a significant association between any prodromal gastrointestinal symptoms (OR=2.30, 95% CI=1.08-4.89, p<0.05) and urinary symptoms (OR=2.54, 95% CI=1.19-5.35, p<0.05) with the PIGD phenotype. PD patients with prodromal gastrointestinal symptoms were thus 2.3 times more likely to develop PIGD phenotype, after controlling for age and LEDD. Similarly, PD participants with prodromal urinary symptoms were 2.5 times more likely to evolve into a PIGD rather than TD phenotype, after controlling for age and LEDD (supplemental material).

**Discussion**

Our study strengths the notion of NMS antedating motor symptoms in PD by assessing the presence and time of onset of the full spectrum of pNMS using a validated NMS questionnaire (NMS-Quest) in a recently diagnosed PD population. Interpretation of previous studies evaluating the frequency and duration of onset of pNMS is limited by study methodological variability; the lack of direct patient evaluation [2], a long duration from PD diagnosis to study enrolment [12], utilisation of non-validated, custom-made NMS questionnaires [13] or studying only limited subsets of the spectrum on pNMS in PD cohorts [14] or 'at risk" of PD cohorts [15,16].

Our study found 90% of participants reporting at least one pNMS while the median number of pNMS experienced was four. Prior studies have reported higher prevalence of prodromal symptoms than our study likely due to methodological differences. A retrospective study conducted via telephone interview with PD patients and controls, using a custom made questionnaire reported a 98.9% of PD subjects having one or more prodromal symptom but this study incorporated prodromal motor symptoms as well as pNMS [2]. Similarly, another retrospective study, with a long mean duration from PD diagnosis of 7.6 ± 5.6 years, reported 98.9% of subjects experienced prodromal symptoms preceding a diagnosis of PD [12].

Based on the Braak model of the hypothesised spread of alpha-synuclein in PD, alpha synuclein accumulation begins in the gut before progressing via the vagus nerve to the brain [17]. Therefore, gastrointestinal (GI) features should be a prominent early manifestation PD. Our study encompassed questions focusing on the GI tract which had not been previously reported, such as the prevalence of prodromal weight loss (7.1%), dysphagia (11.7%) and incomplete bowel emptying (16.9%). Prevalence of prodromal constipation symptoms (24.7%) and hyposmia (35.7%) have previously be reported and are approximately in line with published work [2,13]. Clustering prodromal GI symptoms together revealed 67.5% of PD subjects had one or more GI symptoms antedating motor symptom development in PD which is consistent with the Braak model of early GI involvement in PD. Moreover, GI clusters, as well as urinary tract clusters, of pNMS were significantly associated with PIGD motor phenotype. To the best of our knowledge, no other study has shown an association between prodromal non-motor symptom clusters and early PD motor phenotype.

In contrast to other studies, the prevalence of prodromal memory complaints (32.8%) and unexplained pain (20.8%) in our study is substantially higher compared with prior reported work [12,13]. Meanwhile, the prevalence of apathy (14.8%) and hyperhidrosis (2.6%) is significant lower than in other studies. The variability in reported prevalence rate of pNMS may be due to individual's perception and reporting of NMS. Many NMS progress slowly and are of mild severity, so underappreciated in the early stages [12]. Furthermore, cognitive impairment has also been associated with underestimation of NMS and loss of awareness of hyposmia has been reported to occur in PD-MCI [18]. It is possible cognitive performance may have impacted on symptom recall in our study as mean MOCA score was 25.2 (± 3.7) and previously published work from the ICICLE-PD study showed that among the 5 cognitive domains, memory impairment was the most common domain affected in PD participants at 1.5 SDs below normative values (15.1%) [5]. However, all participants enrolled in the study underwent rigorous assessment to exclude dementia.

Gender has been reported as an independent predictor of NMS reported in early PD studies. Females have been reported to experience more anxiety, pain, depression and sleep disturbance [19-21] while males have been reported to experience more apathy and sexual dysfunction [22-24]. However, there is a paucity of work examining the influence of gender on NMS in the prodromal period. We found gender difference in terms of specific pNMS experienced, namely sexual dysfunction, forgetfulness and dream re-enactment being more prevalent in males, and unexplained weight change and anxiety in females. Gender differences in perceived pNMS prevalence may be reflective of what each gender interprets to be important rather than any underlying early pathological evolutionary difference between the two genders.

There are some limitations in our study. The retrospective design of this study may have introduced recall error and thereby affected the accuracy of the data. Attempts were made to minimise recall errors by having experienced movement disorder physicians conduct face-face interviews with recently diagnosed PD patients including a caregiver interview. Another limitation is the lack of a validated prodromal questionnaire to evaluate pNMS. The NMS-Quest was adapted to identify prodromal NMS as is has been extensively used to investigate NMS in de novo, early PD. However, its sensitivity and specificity for evaluating prodromal symptoms in 'at risk' PD cohorts have not been established. Therefore, it is entirely possible some of the symptoms reported in this study are not related to an evolving Lewy body disorder but other underlying medical conditions or non-specific normal age related symptoms.

In conclusion, our study has shown pNMS are prevalent, antedate motor symptoms in some cases by several years and distinct gender differences exist in the pNMS experienced. Furthermore, prodromal GI and urinary tract symptoms were associated with the PIGD motor phenotype.

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Table 1 Characteristics of patients with Parkinson's Disease

| **Variable** | **PD (n=154)** |
|---|---|
| Gender - Male/Female n(%) | 100 (64.9)/ 54 (35.1) |
| Age (years) | 66.4 (10.4) |
| Duration of PD (months) median(IQR) | 4.7 (2.6 – 8.1) |
| MDS-UPDRSIII | 26.9 ± 12.1 |
| H&Y staging | 2.0 ± 0.7 |
| H&Y Stage n(%) | |
| - I | 35 (22.7) |
| - II | 88 (57.1) |
| - III | 30 (19.5) |
| - IV | 1 (0.6) |
| - V | 0 |
| PD medication treatment n(%) | |
| - Drug naïve | 19 (12.3) |
| - Levodopa | 45 (29.2) |
| - Dopaminergic agonists | 57 (37) |
| - MAOB inhibitor | 73 (47.4) |
| - LEDD (mg/day) | 178.1 ± 148.2 |
| Motor phenotype n(%) | |
| - PIGD | 78 (50.6) |
| - Indeterminate | 13 (8.4) |
| - TD | 63 (40.9) |
| MMSE | 28.6 ± 1.3 |
| MoCA[a] | 25.2 ± 3.7 |
| GDS-15 | 2.8 ± 2.6 |

Figures are mean ± SD unless otherwise stated.
IQR= interquartile range; PIGD = Postural instability gait difficulty motor subtype; TD = Tremor dominant motor subtype; PD= Parkinson's disease; MMSE=Mini Mental state examination; MoCA= Montreal Cognitive Assessment; MDS-UPDRS = Movement Disorder Society – revised Unified Parkinson's Disease Rating scale; LEDD = Levodopa equivalent daily dose; GDS-15 = Geriatric Depression Scale-15; MAOB= Monoamine oxidase B; H&Y= Hoehn & Yahr.
a MoCA completed in 140 patients with PD

Table 2. Prevalence NMS at screening and prodromal non-motor symptoms in PD patients and median duration before the development of motor symptoms

| | pNMS (n=154) | Time interval of non-motor symptom preceding motor symptoms, median months (IQR) | pNMS in males vs. females | | | |
|---|---|---|---|---|---|---|
| | n (%) | | Males (n=100) n (%) | Females (n=54) n (%) | Test Statistic | P-value |
| No. of PD patients with symptoms | 139 (90.3) | | | | | |
| No pNMS experienced median no. (IQR) | 4 (2-7) | | 4 (2-6.25) | 4 (2-7) | U=2850.5 | 0.649 |
| Gastrointestinal Tract | | | | | | |
| Sialorrhea | 47 (30.5) | -33 (-18 to-3) | 34 (34) | 13 (24.1) | $\chi 2$ =1.6 | 0.202 |
| Dysphagia | 18 (11.7) | -25 (-27 to-4) | 11 (11) | 7 (13) | $\chi 2$ =0.1 | 0.718 |
| Nausea | 3 (1.9) | -25 (-48 to-24) | 1 (1) | 2 (3.7) | $\chi 2$ =1.3 | 0.247 |
| Constipation | 38 (24.7) | -108 (-105 to-11) | 24 (24) | 14 (25.9) | $\chi 2$ =0.1 | 0.791 |
| Bowel incontinence | 4 (2.6) | -175 (-516 to-1) | 2 (5) | 2 (3.7) | $\chi 2$ =0.4 | 0.526 |
| Incomplete Bowel emptying | 26 (16.9) | -55 (-31 to-6) | 17 (17 | 9 (16.7) | $\chi 2$ = <0.1 | 0.958 |
| Hyposmia | 55 (35.7) | -148 (-218 to-26) | 32 (32.0) | 23 (42.6) | $\chi 2$ =1.7 | 0.191 |
| Weight change (unexplained) | 11 (7.1) | -13 (-12 to-1) | 4 (4.0) | 7 (13.0) | $\chi 2$ =4.2 | 0.039 |
| Urinary tract | | | | | | |
| Urinary Urgency | 42 (27.3) | -63 (-65 to-12) | 25 (25) | 17 (31.5) | $\chi 2$ =0.7 | 0.389 |
| Nocturia | 29 (18.8) | -82 (-78 to-12) | 18 (18) | 11 (20.4) | $\chi 2$ =0.1 | 0.72 |
| Sexual Function | | | | | | |
| Sexual dysfunction | 24 (15.6) | -89 (-87 to-22) | 22 (22.0) | 2 (3.7) | $\chi 2$ =8.9 | 0.003 |
| Impaired Libido | 15 (9.7) | -56 (-96 to-18) | 12 (12) | 3 (5.6) | $\chi 2$ =1.7 | 0.198 |
| Cardiovascular | | | | | | |
| Orthostatic symptoms | 28 (18.2) | -23 (-31 to-2) | 20 (20.0) | 8 (14.8) | $\chi 2$ =0.6 | 0.426 |
| Falls | 16 (10.4) | -13 (-12 to-2) | 11 (11.0) | 5 (9.3) | $\chi 2$ =0.1 | 0.735 |
| Lower Limb swelling | 17 (11.0) | -61 (-75 to-8) | 10 (10.0) | 7 (13.0) | $\chi 2$ =0.3 | 0.576 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Neuropsychiatric and cognitive | | | | | | |
| Forgetfulness/memory | 50 (32.5) | -36 (-36 to-8) | 38 (38) | 12 (22.2) | $\chi 2$ =4.0 | 0.046 |
| Impaired concentration | 25 (16.2) | -37 (-33 to-8) | 16 (16.0) | 9 (16.7) | $\chi 2$ =<0.11 | 0.915 |
| Anxiety | 42 (27.3) | -99 (-36 to-12) | 22 (22.0) | 20 (37.0) | $\chi 2$ =4.0 | 0.046 |
| Low mood | 27 (17.5) | -20 (-31 to-7) | 15 (15) | 12 (22.2) | $\chi 2$ =<0.1 | 0.261 |
| Loss of interest/ apathy | 22 (14.3) | -20 (-25 to-8) | 13 (13) | 9 (16.7) | $\chi 2$ =0.4 | 0.535 |
| Delusions | 0 (0) | NA | 0 (0) NA | 0 (0) | NA | NA |
| Visual Hallucinations | 12 (7.8) | -12 (-17 to-4) | 7 (7.0) | 5 (9.3) | $\chi 2$ =0.2 | 0.618 |
| Sleep | | | | | | |
| Daytime Somnolence | 32 (20.8 ) | -68 (-79 to-12) | 25 (25) | 7 (13) | $\chi 2$ =3.1 | 0.079 |
| Insomnia | 10 (6.5) | -28 (-51 to-11) | 5 (5) | 5 (9.3) | $\chi 2$ =1.0 | 0.306 |
| Dream re-enactment | 37 (24.0) | -167 (-178 to-16) | 29 (29.0) | 8 (14.8) | $\chi 2$ =3.9 | 0.049 |
| Vivid dream imagery | 35 (22.7) | -175 (-228 to-12) | 25 (25.0) | 10 (18.5) | $\chi 2$ =0.8 | 0.36 |
| Restless legs | 28 (18.2) | -70 (-49 to-6) | 14 (14.0) | 14 (25.9) | $\chi 2$ =3.4 | 0.067 |
| Miscellaneous | | | | | | |
| Diplopia | 11 (7.1) | -112 (-109 to-19) | 6 (6.0) | 5 (9.3) | $\chi 2$ =0.6 | 0.454 |
| Hyperhydrosis | 4 (2.6) | -48 (-93 to-11) | 1 (1.0) | 3 (5.6) | $\chi 2$ =2.9 | 0.090 |
| Pain (unexplained) | 32 (20.8) | -15 (-23 to-6) | 17 (17) | 15 (27.8) | $\chi 2$ =2.4 | 0.116 |

NMS= Non-motor symptoms, pNMS=prodromal non-motor symptoms, PD = Parkinson's disease; IQR = Interquartile range.

Table 3: Prevalence and median duration of Prodromal NMS according to distinct prodromal NMS domains

| Symptom Group | PD pNMS | Time interval of non-motor symptom preceding motor symptoms, median months (IQR) | pNMS in males vs. females | | | |
|---|---|---|---|---|---|---|
| | n (%) | | Males (n=100) n (%) | Females (n=54) n (%) | $\chi 2$ | p-Value |
| Gastrointestinal Tract | 104 (67.5) | - 58.5 (-217 to -16) | 67 (67.0) | 37 (68.5) | <0.1 | 0.848 |
| Urinary tract | 65 (42.2) | -45 (-126 to -14) | 38 (38.0) | 20 (37.0) | <0.1 | 0.906 |
| Sexual function | 32 (20.8) | -60 (-119 to -29) | 26 (26.0) | 3 (5.6) | 9.6 | 0.002 |
| Cardiovascular | 50 (32.5) | -12 (-48 to -5) | 35 (35.0) | 15 (27.8) | 0.8 | 0.361 |
| Neuropsychiatric and cognitive | 19 (12.3) | -39 (-132 to-14) | 55 (55) | 30 (55.6) | <0.1 | 0.947 |
| Sleep | 81 (52.6) | -66 (-237 to-19) | 55 (55.0) | 25 (46.3) | 1.1 | 0.302 |
| Miscellaneous | 34 (22.1) | -12 (-48 to-8) | 19 (19.0) | 22 (40.7) | 8.5 | 0.004 |

NMS= Non-motor symptoms, pNMS= prodromal non-motor symptoms, PD = Parkinson's disease; IQR = Interquartile range

Table 4. Demographics and Prevalence of Prodromal Non-Motor Symptoms among PD Motor Subtypes

| Variable | PIGD (n=78) | TD (n=63) | Test statistic | P Value |
|---|---|---|---|---|
| Gender Male /Female n(%) | 56(71.8)/ 22(28.2) | 36(57.1)/27(42.9) | $\chi 2$= 3.3 | 0.069 |
| Age | 68.4 (9.2)1 | 63.6 (10.97)3 | t=2.7 | 0.007 |
| Duration of PD (months) | 6.2 (4.8) | 5.7 (4.4) | U=2376.0 | 0.737 |
| LEDD (mg/day) | 203.04 ± 138.61 | 151.4 ± 165.4 | U=1684.5 | 0.001 |
| MMSE | 28.53 (1.3) | 28.8 (1.3) | U=2081.0 | 0.106 |
| MoCAa | 24.77 (3.6) | 25.6 (3.7) | U=1709.0 | 0.117 |
| GDS-15 | 3.12 (2.4)3 | 2.3 (2.3)1 | U=1849.5 | 0.011 |
| MDS-UPDRS III | 26.96 (12.1) | 26.2 (12.1) | U=2315.0 | 0.556 |

Figures are mean(SD) unless otherwise stated. Significant results are highlighted in bold. Abbreviations: PIGD = Postural instability gait difficulty motor subtype; TD = Tremor dominant motor subtype; PD= Parkinson's disease; MMSE= Mini-Mental state examination; MoCA= Montreal Cognitive Assessment; MDS-UPDRS = Movement Disorder Society – revised Unified Parkinsons' Disease Rating scale; LEDD = Levodopa equivalent daily dosag; GDS-15 = Geriatric Depression Scale-15.

a MoCA completed in 140 patients with PD