

# Study on Gender Specific Variability of Gastrointestinal, Genitourinary and Depression Related Non Motor Symptoms of Parkinson Disease

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## Abstract

**Introduction:** Parkinson's disease is a second most common neurodegenerative disorder after Alzheimer's disease. It affects 1% of population over age of 50 years. Three main features of PD is asymmetric onset of bradykinesia, rigidity and resting tremors. Non motor symptoms are common in patients of Parkinson's Disease. These remain undiagnosed most of the time. **Aim and Objectives:** To analyse gender specific, age related and demographic variability of non motor symptoms (Gastrointestinal, genitourinary and depression related symptoms) of Parkinson's disease. **Material and Methods:** Present study Included 100 cases (65 Males and 35 Females) of Parkinson's disease presenting at department of neurology, Dayanand Medical College and hospital, Ludhiana. 30 questionnaire of non motor symptoms in hindi and Punjabi were given to patients. Gender, age, duration of non motor symptoms, Parkinson's phenotype and complete demographic profile of each patient taken into account for study. Thereafter results were statistically analysed for all parameters. **Conclusion:** It is concluded that mean age and duration of non-motor symptoms were higher in males as compared to females. GI symptoms amongst non-motor symptoms were commonest and amongst GI symptoms constipation was most common and there was positive correlation of H&Y with age and non motor symptoms especially gastrointestinal, genitourinary and depression related symptoms.

**Keywords:** Gender Specific Variability, Non Motor Symptoms of Parkinson, Parkinson's disease

## 1. Introduction

Parkinson's disease is second most common neurodegenerative disorder after Alzheimer's disease<sup>[1]</sup>. It affects 1% of the population over age of 50 years. The typical hall mark features of PD are asymmetric onset of bradykinesia, rigidity and resting tremors.<sup>[2]</sup> The peak age of PD is early 5<sup>th</sup> decade and duration of its course range from 10-25years.<sup>[3]</sup> The disease is caused by loss of dopaminergic neurons in substantianigra of midbrain.<sup>[4]</sup> Various non motor symptoms also occur in PD and these are often overshadowed by motor symptoms.<sup>[5]</sup> James

Parkinson's was the first who noticed various non motor symptoms like constipation, dysphagia, sleep disturbance and urinary incontinence etc in 1817.<sup>[6]</sup> Later numerous studies have indicated that non motor symptoms are frequently accompanied motor symptoms.<sup>[5]</sup> One of the study reported that existed depression are not identified by neurologist in over 50% of consultations for PD.<sup>[7]</sup> 21% of PD patients presents with NMS which includes pain, depression, anxiety and urinary dysfunctions etc. NMS can present at any stage.<sup>[8]</sup> Despite the importance of NMS in PD, there is very scant data present on various parameters of NMS in Indian context.

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## 2. Aims and Objectives

- To analyse the demographic and age related variability in gastrointestinal, genitourinary and depression related NMS of Parkinson's disease.
- To analyse the gender specific variability of gastrointestinal, genitourinary and depression related symptoms.

## 3. Material and Methods

### 3.1 Source and Method of Collection of Data

The present study included 100 OPD (65 males and 35 females) cases of idiopathic PD from different demographic backgrounds and of both genders of different age group (35-85yrs) enrolled with Department of Neurology, Dayanand Medical College and Hospital, Ludhiana. Patients satisfying the UK PD brain bank criteria for idiopathic Parkinson disease were included in study.

## 4. Validation of Data

In this present study total 100 patients with diagnosis of Parkinson disease were screened. An independent professional translated the items and another translated to response categories in Punjabi/Hindi. Then a consolidated forward version was produced. This questionnaire then was again translated into English by another professional to check for differences between Hindi/Punjabi version and the original questionnaire. After a careful review few changes were made and provisional version of questionnaire was finalized. Subsequently this questionnaire was pilot tested and administered to a sample of 20 patients of Acute Coronary syndrome. After pilot testing a few more changes were made. Then a final version of scale was provided and used in the study. 20 healthy individuals were included as the controls, preferably the family members with similar age groups.

## 5. NMSS (Non Motor Symptoms Study)

The NMSS includes ten domains and total of 30 questions including 10 questions related to GIT, GUT and depression related symptoms. Present study concerned

with Gastrointestinal, Genitourinary and depression related symptoms. NMSS not only assesses whether or not, NMS present but also rates their frequency (0-4) and severity (0-3). If the product of the frequency and severity is 1 or greater, then 1 point is assigned.

The NMSS was specifically designed for the patients to help them in assessing their own symptoms; thus, it was not specifically constructed for care giver's assessment of their patients. The mean of each were taken. Patient individual symptoms were compared with respect to age, gender, H&Y (Hoehn and Yahr) stage, disease duration and subtype (akinetic/tremor predominant).

## 6. Exclusion Criteria

Patients with following diagnosis were excluded from study

- Multisystem atrophy
- DSM 4 criteria of depression
- Corticobasilar degeneration
- Dementia
- Dementia with lewy body disease
- Progressive supranuclear palsy
- Fronto-temporal dementia
- History of repeated head injury

## 7. Parkinson Disease Non Motor Symptoms (PDNMS) Questionnaire

A range of problems listed below were asked for presence/once present and rate them with frequency and severity. The maximum severity and frequency number was 12 and 0 for minimum. Further the NMS symptoms were subdivided into various groups as shown below. The complete NMS questionnaire data was obtained and compared between gender match group and statistical analysis with spearman coefficient for correlation was done.

## 8. Ethical Approval

Ethical approval was obtained from the institutional review board of Dayanand medical college and hospital after submission of study proposal and design.

## PDNMS questionnaire

NMS SUBTYPE	SYMPTOMS	YES		NO	
		Frequency (0-4)	Severity (0-3)	(0-4)	(0-3)
<b>Gastro intestinal symptoms</b>	Dribbling of saliva during daytime Loss or change in your ability to taste or smell, Diffuculty swallowing food or drinks Vomiting or feeling of sickness Constipation(less than 3 bowel movements a week) Bowel incontinence Feeling bowel emptying is incomplete after having being to toilet				
<b>Genito Urinary Symptoms</b>	A sense of urgency to pass urine makes you to rush to the toilet Getting up regularly at night to pass urine				
<b>Depression Related Symptoms</b>	Feeling sad Low or blue				

## 9. Statistical Analysis

Spearman's correlation used to analyse correlation of symptoms of Parkinson. It was calculated using Microsoft excel software for calculation purposes.

- Calculation of rho was done. P value was calculated for significance.
- RATIO OF TREMOR/AKINETIC STATE- Ratio were calculated. If the ratio is more than 0.8 then patient is classified as having tremor prominent. If the ratio less than 0.8 then patient is akinetic dominant.

## 10. Observations and Results

In present study it was observed that mean age and duration was higher in males than females. The mean age

for males was  $61.86 \pm 10.14$  years and for females it was  $57.09 \pm 8.576$  yrs. The mean H&Y score was  $2.66 \pm 0.802$  and PD duration of disease was  $42.51 \pm 33.7$  months for females whereas for males H&Y score  $2.40 \pm 0.746$  and PD duration was  $61.86 \pm 10.14$ . The mean H&Y score was comparable between both groups. With regard to PD phenotype there were 88 patients' akinetic dominant and 12 patients was from tremors predominant phenotype in total cohort. The mean NMS in males was  $81.58 \pm 51.34$  and  $75.37 \pm 45.97$  in females (Table 1).

In our study there was definitive difference between males and females. Males were having more symptoms as compared to females; this may be due to higher age and duration of the disease of PD. Gender specific NMS depicted in (Table 2) below.

The non motor symptoms like feeling of incomplete bowel evacuation, vomiting or feeling of sickness and feeling sad or blue had higher mean  $\pm$ SD in females.

**Table 1.** Mean  $\pm$  Sd of age/H&Y score/PD duration (N=100)

	MALE (N= 65)	FEMALE (N=35)	p VALUE
	MEAN $\pm$ SD	MEAN $\pm$ SD	
AGE (YEARS)	$61.86 \pm 10.14$	$57.09 \pm 8.576$	$p > 0.05$
H&Y	$2.40 \pm 0.746$	$2.66 \pm 0.802$	$p > 0.05$
PD DURATION (MONTHS)	$61.86 \pm 10.138$	$42.51 \pm 33.7$	$p > 0.05$
< 0.8 AKINETIC	58	30	$p > 0.05$
$\geq 0.8$ TREMOR PREDOMINANT	8	4	$p > 0.05$
NMS	$81.58 \pm 51.34$	$75.374 \pm 45.97$	$p > 0.05$

**Table 2.** Percentage and number (frequency) of gender specific non motor symptoms

NON MOTOR SYMPTOMS	GENDER (frequency)			
	FEMALE		MALE	
	No. & %		No & %	
GASTROINTESTINAL SYMPTOMS (1-6)	2	(5.7%)	2	(3.1%)
GENITOURINARY SYMPTOMS (7-8)	7	(20.0%)	17	(26.2%)
DEPRESSION RELATED SYMPTOMS (9-10)	10	(28.6%)	15	(23.1%)

Whereas in males the non motor symptoms which were noted higher mean±SD include gastrointestinal symptoms (loss or change in your ability to taste or smell, difficulty in swallowing or drinking etc) except above mentioned GI symptoms, sense of urgency of urine. While mean±SD almost equal in case of symptoms like getting up regularly at night to pass urine and dribbling of saliva.

We further separately analysed the individual NMS with respect to demographic parameter to find a correlation of these.

The NMS such as loss of ability to taste or smell constipation and bowel incontinence had positive correlation with increasing age and disease severity (H&Y stage) which were found to be statistically significant (p<0.05). Though these symptoms were not

having any direct correlation with disease duration and the phenotype of Parkinson disease, as the age of patient with Parkinson disease increases the number of the NMS increases, similarly as the H&Y stages increases, NMS increases in frequency and severity.

Whereas symptoms like dribbling of saliva and feeling sad had positive correlation only with H&Y stage that is as the stage increases the frequency and severity of disease increases (p<0.05). There was no correlation with age, duration and subtype. Other non motor symptoms like vomiting, feeling of incomplete bowel evacuation, sense of urgency and nocturia had no correlation with age/H & Y stage/ Parkinson duration (Table 3, 4).

Hence above table showed that there was significant correlation of age and H&Y stage with many gastrointestinal

**Table 3.** Symptoms spearman rho correlation with age/H&Y/PD duration and Parkinson phenotype predominant (N=100)

	Spearman's rho coefficient of Age (yrs)	p value	H & Y stage	p value	Tremor/ Akinetic	p value	Duration in months	P value
Dribbling of saliva during daytime	.171	.089	.233*	.020	.103	.307	-.504	.594
Loss or change in your ability to taste or smell	.212*	.035	.135	.180	-.071	.485	-.087	.389
Difficulty swallowing or drinking	.290**	.003	.250*	.012	-.003	.978	-.031	.759
Vomiting	-.151	.134	.000	1	-.045	.658	-.114	.257
Constipation	.346**	.001	.298**	.003	.133	.187	-.031	.759
Bowel incontinence	.209	.037	.269**	.007	.111	.272	.106	.293
Feeling of incomplete bowel evacuation	.145	.150	.013	.899	.075	.460	-.260**	.009
Sense of urgency to pass urine	-.051	.613	.124	.217	.022	.831	.148	.141
Getting up regularly in night for passing urine	.085	.401	.126	.213	-.036	.719	-.048	.635
Feeling blue or sad	.161	.109	.334**	.001	.177	.078	.046	.650

\*\* Correlation is significant at the 0.01 level (2- tailed)

\* Correlation is significant at the 0.05 level (2- tailed)

**Table 4.** Spearman rho correlation table of symptom phenotype with age and H&Y stage

Non motor symptoms	Spearman's rho coefficient of Age (yrs)	P value	Spearman's rho coefficient of H&Y	P value
Gastro intestinal symptoms	.348 **	.0001	.357**	.0001
Genitourinary symptoms	.022	.829	.157	.118
Depression related symptoms	.071	0.484	.247*	.013

\*\*Correlation is significant at the 0.01 level (2- tailed)

\*Correlation is significant at the 0.05 level (2- tailed)

symptoms whereas only feeling of incomplete evacuation significantly correlated with duration of Parkinson's disease.

## 11. Discussion

In our study of 100 patients with Parkinson disease there were 65 males with mean age of 61.86 yrs and 35 females with a mean age of 57.09 yrs. This mean age is comparable to the study done by chaudhary et al.,<sup>[9]</sup> in which mean age of 123 patients was 56.5. The mean NMS score was 75.77±45.97 in females, in males the mean NMS score was 81.58±51.34 and mean H&Y score was 2.66 in females and 2.40 in male which was comparable with other study done by lolekha P<sup>[10]</sup> in which the H&Y of 83 patients was 2.36.

There was no difference in our study with respect to duration, H&Y type and age of onset of PD. The maximum number of non motor symptoms reported were between (28.6%) in females and (23.1%) in males similar to study done by Ravan et al.<sup>[11]</sup> The difference between gender can be due to advance disease age. The difference between the genders with respect to mean was not significant. These results were consistent with those of Song et al.<sup>[12]</sup>

The comparison between males and females gastrointestinal symptoms to be the most common NMS and constipation was most common symptom among these. Constipation most common in males (4.14±3.47) as compare to females (3.63±3.92). Feeling of incomplete bowel evacuation was most common NMS symptoms in females with mean of 4.00±3.76 and it was 3.38±3.43 in males. Feeling of incomplete bowel evacuation can be due to constipation as such similar to study of chaudhary et al.<sup>[9]</sup> Previous study done by cheng et al.,<sup>[13]</sup> reported similar pattern of complaints among patients of Parkinsons disease and normal elderly population. Krishna et al.,<sup>[14]</sup> also found GIT dysfunction and sadness being the most common non motor symptoms and more in females.

This study found significant correlation in group analysis of gastrointestinal domain, genitourinary and depressive symptoms. Dribbling of saliva, constipation, loss of smell and taste had positive correlation with age and H&Y stage. As the age and stage of Parkinson disease increases the frequency and severity of symptoms increases.

In study done by Ozge et al.,<sup>[15]</sup> showed most common symptoms were dribbling of saliva and constipation. PRIAMO study reported fatigue, anxiety and insomnia as most common symptoms followed by urinary complaints and difficulty in concentration.<sup>[16]</sup>

This is an important finding in our study, signifying the increasing burden of NMS with disease advancement and severity. In our study, the subgroup analysis revealed that the NMS such as GI symptoms, genitourinary symptoms and depression worsened with advancing age and H&Y stage of motor symptoms.

Parkinson disease having non motor symptoms it was highlighted by Shulman et al.,<sup>[17]</sup> and chaudhary et al.,<sup>[9]</sup> although there were less no of patients in both the groups. Depression related symptoms were higher in females as compare to males. These were highlighted by chaudhary et al., but we compared the male and female mean depression related NMS score which was higher in females as compared to males.

## 12. Conclusion

In our study we have seen that there was a positive correlation of H&Y with age and non motor symptoms especially gastrointestinal, genitourinary and depression related symptoms. There was no correlation of duration and phenotype of Parkinson subtype with the non motor symptoms. There was difference between non motor symptoms in males and females. Females have more depression related symptoms as compared to males.

In males gastrointestinal symptoms and among these constipation was most common in frequency as well as severity in relation to feeling sad, low or blue was most common symptom in females. Severity of GI symptoms was more common in males as compared to females although it was not statistically significant. Non motor symptoms can occur in significant variation with respect to gender, age and H&Y stages. There was difference between the dominant symptoms between males and females.

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