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# Factor Associated with Orthostatic Hypotension in Parkinson's Disease

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**ABSTRACT**

**Introduction:** Orthostatic hypotension (OH) affect approximately 30% of patients with Parkinson's disease (PD). This condition not only reduces quality of life but is also associated with increased mortality. OH has been shown to double the risk of falls in the elderly, worsens motor function, and accelerate cognitive decline. There has been limited study into the prevalence and contributing factors of OH in Parkinson's disease patients in Indonesia. **Objective:** This study aimed to determine factors associated with OH in patients with Parkinson's disease. The variables analyzed included age, sex, duration of PD, disease stage based on the Hoehn and Yahr scale, levodopa equivalent dose (LED), the length of antiparkinsonian agents use, MoCA Ina (Montreal Cognitive Assessment Indonesian version) score, comorbid conditions, use of antihypertensive agents, and body mass index (BMI). **Methods:** This is a descriptive-analytic study with a cross-sectional design. The study population consisted of all Parkinson's disease patients who visited the neurology polyclinics at two hospitals in Palembang. Patients were selected based on specific inclusion and exclusion criteria. To discover associations, bivariate and multivariate analyses were performed. **Results:** The study involved 41 patients with PD at Mohammad Hoesin Hospital and Pusri Medika Hospital in Palembang, from June to December 2024. OH, was found in 43.9% of PD patients, most of whom reported symptoms. Bivariate and multivariate analyses revealed no significant associations between OH and factors such as comorbidities, the length of antiparkinsonian medication use, total LED, age, sex, duration of PD, disease stage (Hoehn and Yahr scale), and of the use of antihypertensive agents. However, underweight BMI was significantly associated with OH in PD patients (p = 0.002, OR = 34.571, 95% CI: 3.77–317.28). **Conclusion:** Underweight was identified as a significant associated factor for OH in PD patients.

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## INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder characterized by impaired brain function due to the degeneration of the substantia nigra pars compacta (SNc) within the basal ganglia. Resting tremor, muscle and joint rigidity, bradykinesia, postural instability, and eosinophilic cytoplasmic inclusion (Lewy bodies) are among the hallmark motor signs of Parkinson's disease.[1] In addition to these typical motor symptoms, non-motor symptoms such as neuropsychiatric disturbances, sleep disorders, sensory abnormalities, gastrointestinal issues, and autonomic dysfuntion may also be observed.[2]

One of the most aggravating symptoms of autonomic dysfunction is orthostatic hypotension (OH). According to the American Academy of Neurology (AAN) and the American Autonomic Society (AAS), OH is defined as a reduction of at least 20 mmHg in systolic blood pressure or 10 mmHg in diastolic blood pressure within three minutes of standing or head tilted 60 degrees. OH can impair perfusion to the other organs, especially the brain. There are two types of OH: non-neurogenic orthostatic hypotension and neurogenic orthostatic hypotension. The type associated with PD is neurogenic orthostatic hypotension.[3]

A meta-analysis estimated the prevalence of OH to be around 30% in PD.[4] The prevalence of OH increases with age and duration of PD. Although Oh is common in PD, only about one-third of affected individuals (16%) present with symptomatic organ hypoperfusion.[3] Bae *et al* reported that OH, as a non-motor symptom, is typically found in the advanced stage; however, it was also detected in 40% of untreated patients in the early stage of the disease.[5,6] A study by Umehara *et al*. was mentioned that the presence of OH in-early stage of PD may indicate a progressive subtype of PD (known as diffuse malignant). This finding is believed to occur due to the involvement of alpha synuclein in sympathetic dopaminergic and noradrenergic structures.[7]

OH has indirect impact on patients' quality of life with PD since it increases likelihood of falls, more severe motor function impairment, and early cognitive decline. Therefore, determining the incidence rate and understanding the factors associated with the development of OH in PD patients is crucial.

## OBJECTIVE

This study aimed to determine factors associated with orthostatic hypotension (OH) in Parkinson's disease (PD). The factors analyzed included age, sex, duration of PD, disease stage based on the Hoehn and Yahr (H&Y) scale, levodopa equivalent dose (LED), the length of antiparkinsonian agents use, MoCA Ina (Montreal Cognitive Assessment Indonesian version) score, comorbid conditions, use of antihypertensive agents, and body mass index (BMI).

## METHODS

This is a cross-sectional observational analytic study utilizing primary data from interviews, physical examinations, and blood pressure measurements conducted at the neurology polyclinics of Mohammad Hoesin Hospital and Pusri Hospital in Palembang from June to December 2024. Blood pressure was measured using an automated sphygmomanometer placed at heart level on the arm. Measurements were taken twice: first in the supine position and then after three minutes of standing.

The study population and sample were all Parkinson's disease (PD) patients who visited the neurology polyclinics of Mohammad Hoesin Hospital and Pusri Hospital Palembang during the study period. A total sampling method was used, including all PD patients who met the inclusion criteria. For those unable to attend the hospital, examinations were conducted during home visits. Inclusion criteria for this study were PD patients diagnosed according to the United Kingdom Parkinson's Disease Brain Bank Criteria and who provided informed consent, either by patient or family. Parkinson's patients who were uncooperative, unable to stand with assistance, or had wounds in the upper arm area (the location of blood pressure measurement) were excluded from the study.

The variables assessed included age, sex, educational level, body mass index (BMI), disease stage of PD (Hoehn and Yahr scale), disease duration, total LED (Levodopa Equivalent Dose), the length of antiparkinsonian agents, MoCA Ina (Montreal Cognitive Assessment-Indonesian version) score, comorbid conditions related to OH, and the use of antihypertensive agents. Based on WHO classification, BMI is divided into underweight, ideal, overweight, and obesity. This study used Hoehn and Yahr staging for assessed Parkinson's disease severity. Stage 1 is defined by unilateral involvement symptoms and minimal functional impairment; Stage 2 characterized by bilateral involvement symptoms without balance impairment; Stage 3 is marked by postural instability and slowed physical movement, though patients remain physically independent; Stage 4 indicates severe disability, patients still able to walk and stand unassisted but require significant assistance for daily activities; and Stage 5 describes a bedridden condition. LED is a formula for calculating the total dose of antiparkinson medication administered to people with PD.

Data processing consisted of data editing, coding, and recording in Microsoft Excel tables. The data were then analyzed using univariate analysis to determine

demographic characteristics, orthostatic hypotension, and the severity of PD. The data were presented in tabular form, with numerical distributions expressed as mean ± standard deviation (SD) or median (minimum-maximum). Normality tests were performed using the Kolmogorov-Smirnov test (n > 50) or Shapiro-Wilk test (n < 50). Categorical data distributions were presented as frequencies and percentages [n (%)].

Statistical analyses were conducted using SPSS for Windows, with descriptive data presented through univariate analysis. Bivariate analysis was done using the chi-square test to assess the association between independent and dependent variables in categorical data, and t-tests were used to compare mean differences in numerical data. Multivariate analysis using logistic regression was conducted to evaluate the most significant variables. A significance level was set at $p < 0.05$.

The study was approved by the Ethical Committee of Dr. Muhammad Hoesin Hospital Palembang on April 27th, 2023, with certification number: DP.04.03/ D.XVIII.6.11/ETIKRSMH/13/2023.

## RESULTS

### Demographic and clinical characteristics

In this study, 41 patients with Parkinson's disease (PD) who met the inclusion criteria were obtained. The mean age of the subjects was 60.56 ± 6.542 years. The sample consisted of 18 women (43.9%) and 23 men (56.1%). Based on educational level, 16 subjects (39%) had college education. According to BMI classification, the majority of subjects (31.7%) has ideal BMI.

Based on the clinical characteristics in this study, 4 subjects (9.8%) were classified as having stage 1 PD, 11 subjects (26.8%) as stage 2, 13 subjects (31.7%) as stage 3, 11 subjects (26.8%) as stage 4, and 2 subjects (4.9%) as stage 5, according to the Hoehn and Yahr scale. The median duration of PD in the subjects of this study was 5 years (0.5–20). The mean total LED was 531 ± 238 mg, and the median length of antiparkinson agents use was 4 yeas (0–15) . Cognitive function was assessed using the MoCA-Ina (Montreal Cognitive Assessment-Indonesian version), with a median value of 19 (13–30). Several comorbidities were also found, including the use of antihypertensive agent in 15 subjects (36.6%), a history of diabetes mellitus in 5 subjects (12.2%), and no reported comorbidities in 21 subjects (51.2%). Among those using antihypertensive agents, 7 subjects (17.1%) used ACE inhibitors/ARBs, 10 subjects (24.4%) used calcium channel blockers (CCB), 1 subject (2.4%) used beta-blockers, and 2 subjects (4.9%) used diuretics.

The incidence of orthostatic hypotension (OH) among patients with PD was 43.9%. Among the 18 subjects who experienced OH, 33.3% were classified as having symptomatic OH. The most commonly reported symptoms included head and neck discomfort, dizziness, and fatigue.

The mean age of group OH and non-OH at PD about 64.04±5.995 vs 60.17 ±7.050 (Tabel 1). OH was equally distributed between sexes, with 9 women (21.9%) and 9 men (21.9%) affected. In contrast, non-OH was more commonly found in men (14 persons, 34.14%) than in women (9 persons, 21.9%). Regarding educational background, the majority of PD patients with OH had a college education (10 persons, 17.1%), whereas the most common education level in the non-OH group was senior high school (7 persons, 17.1%). BMI classification showed that OH was more common among underweight subjects (11 persons,26.8%), while non-OH was more common in those with an ideal BMI (11 persons, 26.8%). The duration of Parkinson's disease in this study revealed similar median values for the OH and non-OH groups: 5 years (0.8–16 years) vs. 5 years (0.5–20 years). The late-onset category was more common among Parkinson's disease patients in the non-OH group, with 17 persons (41.5%), compared to 12 persons (29.3%) in the OH group. Age of onset refers to the age at which the patient was first diagnosed with Parkinson's disease. In the early-onset category, both the OH and non-OH groups included 6 persons (14.3%) each. The OH group got a higher total levodopa equivalent dose in the OH group was (604 ± 250 mg) than the non-OH group (473 ± 217 mg). Meanwhile, regarding the MoCA-Ina scores in Parkinson's disease patient with OH, the median value was 18, the minimum was 13 and the maximum was 29. In non-OH group, the median value was 21, with a minimum of 13 and a maximum of 60.

Table 1. Demographics and clinical characteristics of Parkinson's disease patients with OH and non-OH

| Characteristics | OH (Mean ± SD/Median (min-max/N (%) | OH (Mean ± SD/Median (min-max/N (%) |
|---|---|---|
| **Age** | 64.04 ± 5.995 years old | 60.17 ± 7.050 years old |
| **Sex** | | |
| - Woman | 9 (21.9%) | 9 (21.9%) |
| - Man | 9 (21.9%) | 14 (34.14%) |

Table 1 continued. Demographics and clinical characteristics of Parkinson's disease patients with OH and non-OH

| Characteristics | OH (Mean ± SD/Median (min-max/N (%) | OH (Mean ± SD/Median (min-max/N (%) |
|---|---|---|
| **Education level** | | |
| - Elementary school | 2 (4.9%) | 5 (12.2%) |
| - Primary high school | 0 (0%) | 5 (12.2%) |
| - Senior high school | 6 (14.6%) | 7 (17.1%) |
| - College | 10 (24.4%) | 6 (14.6%) |
| **BMI** | | |
| - Underweight | 11 (26.8%) | 1 (26.8%) |
| - Ideal | 2 (4.9%) | 11 (4.9%) |
| - Overweight | 3 (7.3%) | 4 (7.3%) |
| - Obesity | 2 (4.9%) | 7 (4.9%) |
| **Duration of Parkinson's disease** | 5 (0.8 – 16) years | 5 (0.8 – 16) years |
| **Total LED** | 604 ± 250 mg | 473 ± 217 mg |
| **The length of use antiparkinsonian agents** | 4.5 (0.4 – 15) years | 4.5 (0.4 – 15) years |
| **MoCA Ina Score** | 18 (13-29) | 21 (13-61) |
| **Comorbid condition** | | |
| - Dehydration | 0 (0%) | 0 (0%) |
| - Bleeding | 0 (0%) | 0 (0%) |
| - CHF | 0 (0%) | 0 (0%) |
| - Using of TCA | 0 (0%) | 0 (0%) |
| - Using of antihypertensive agents | 7 (17.1%) | 8 (19.5%) |
| - History of diabetes melitus | 0 (0%) | 5 (12.2%) |
| - Without comorbid | 11 (26.8%) | 10 (24.4%)%) |
| **Antihypertensive agent category** | | |
| - ACEI/ARB | 1 (2.4%) | 6 (14.6%) |
| - CCB | 6 (14.6%) | 4 (9.8%) |
| - Beta blocker | 0 (0%) | 1 (2.4%) |
| - Diuretic | 1 (2.5%) | 1 (2.5%) |

BMI, Body Mass Index; PD, Parkinson's Disease; LED, Levodopa Equivalent Dose; CHF, Congestive Heart Failure; TCA, Tricyclic Antidepressant; ACEI, Angiotensin Converting Enzyme Inhibitors; Angiotensin Receptor Blocker; CCB, Calcium Channel Blocker

Table 2. Bivariate analytic of clinical characteristics between Parkinson's disease patients with OH and non-OH

| | OH | non-OH | p-value | OR (95% CI) |
|---|---|---|---|---|
| **Onset of age** | | | | |
| - Late onset | 12 | 17 | 0.613 | 0.706 (0.183-2.727) |
| - Early onset | 6 | 6 | | |
| **Sex** | | | | |
| - Woman | 9 | 9 | 0.486 | 1.556 (0.447-5413) |
| - Man | 9 | 14 | | |
| **BMI** | | | | |
| - Underweight | 11 | 1 | 0.002 | 34.571 (3.767-317.234) |
| - Non-underweight | 7 | 22 | | |
| **Total LED** | | | | |
| - ≥ 600 | 11 | 9 | 0.166 | 2.444 (0.690-8.657) |
| - < 600 | 7 | 14 | | |
| **Duration of PD** | | | | |
| - ≥ 5 years | 10 | 12 | 0.828 | 1.146 (0.332-3.953) |
| - < 5 years | 8 | 11 | | |
| **Stage of PD (H&Y)** | | | | |
| - ≥ stage 3 | 13 | 13 | 0.304 | 2.000 (0.534-7.490) |
| - < stage 3 | 15 | 10 | | |

Table 2 continued. Bivariate analytic of clinical characteristics between Parkinson's disease patients with OH and non-OH

| | OH | non-OH | p-value | OR (95% CI) |
|---|---|---|---|---|
| **The length of use antiparkinsonian agents** | | | | |
| - ≥ 5 years | 8 | 7 | 0.206 | 2.286 (0.634-8.234) |
| - < 5 years | 9 | 1 | | |
| **Comorbidities** | | | | |
| - Yes | 6 | 14 | 0.080 | 0.321 (0.089-1.167) |
| - No | 12 | 9 | | |

Based on Table 2, several variables had p-value < 0.25. These variables were then included in a multivariate analysis to assess the strength of the relationship between the independent variables and the incidence of OH in PD patients. BMI, total LED, the length of antiparkinsonian agent use, and comorbid conditions met the criteria for inclusion in the multivariate analysis.

Table 4. Multivariate analytic of clinical characteristic between Parkinson's disease patients with OH dan non-OH

| | | p-value | OR | 95% CI |
|---|---|---|---|---|
| Step 1 | Comorbid condition | 0.661 | 0.689 | 0.130-3.646 |
| | The length of use antiparkinsonian agents | 0.990 | 1.011 | 0.177-5.778 |
| | Total LED | 0.322 | 2.365 | 0.430-12.988 |
| | BMI | 0.004 | 32.079 | 3.119-329.930 |
| Step 2 | Comorbid condition | 0.657 | 0.688 | 0.132-3.593 |
| | Total LED | 0.309 | 2.370 | 0.450-12.489 |
| | BMI | 0.003 | 32.171 | 3.269-316.556 |
| Step 3 | Total LED | 0.252 | 2.576 | 0.510-13.008 |
| | BMI | 0.002 | 35.314 | 3.69-337.910 |
| Step 4 | BMI | 0.002 | 34.571 | 3.76-317.23 |

Logistic regression was used in multivariate analysis (Table 3) to identify which independent variables were most strongly associated with the related variables. Underweight BMI was found to be significantly associated with OH (p = 0.002; OR = 34.571, 95% CI: 3,76 - 317.23).

## DISCUSSION

A total of 43.9% of the study subjects had orthostatic hypotension (OH), while 56.1% were non-OH. These findings are consistent with several previous cross-sectional studies by Palma *et al*, which reported the incidence of OH in patients with Parkinson's disease (PD) renged from 30 to 50%.[3] A meta-analysis also revealed that the prevalence of OH in PD was around 9.6 to 64.9%.[4] OH occurs due to the failure of the autonomic nervous system to regulate blood pressure in response to postural changes, as a result of inadequate norepinephrine (NE) release from postganglionic sympathetic nerves. OH in PD is mostly caused by postganglionic sympathetic denervation, which impairs the efferent baroreflex response, leading to neurogenic OH. In contrast, non-neurogenic OH induced by intravascular volume depletion, medications, or heart failure, can also contribute to OH in PD.[8]

In this study, 18 patients had orthostatic hypotension, with 6 (33.3%) of them were symptomatic. Reported symptoms included head and neck discomfort, dizziness, and fatigue. Previous studies have noted that not all patients experience symptoms of organ hypoperfusion; approximately one-third are symptomatic, while the others are asymptomatic.[9]

The average age of OH and non-OH in PD patients was 64.04±5.995 vs 60.17±7.050, respectively (Table 3). A study by Umehara *et al* stated that PD patients who suffered OH had an average age (±SD) of 70.6 ± 8.9 years.[7] Advanced age is a contributing factor in the occurrence of OH among PD patients. As people get older, the sensitivity of the carotid sinus and baroreflex sensors in the aortic arch decreases, elasticity of blood vessels decreases, and degeneration of the sympathetic nervous system occurs, all of which contribute to the development of OH.[10]

In this study, OH was found in 9 (21.9%) PD patients, with an equal distribution for female and male subjects. Meanwhile, non-OH in PD was more common in males, occuring in 14 male subjects (34.14%) compared to 9 female subjects (21.9%). In a

study conducted by Centi *et al.*, the ratio of male to female PD patients experiencing OH was 11:7. Meanwhile, a cross-section study by Hommel *et al.* found that 56.3% of PD patients with OH were female.[11] Additionlly, Hiorth *et al*. found that among PD patients with OH, 18 (52.9%) were male and 16 (47.05%) were female.[12] The mechanism underlying the association between gender and the occurrence of OH in PD has not fully understood.

The median duration of Parkinson's disease in this study for the OH and non-OH groups were quite similar: 5 years (0.8–16 years) vs. 5 years (0.5–20 years), respectively. In contrast by Umehara *et al*. reported the disease duration of PD patients who experienced OH was 1.5±1.5 years.[7] The prevalence of OH in PD has been shown to increase with both age and disease duration, although other studies state that a decrease in blood pressure may occur at all stages of disease.[13] Late-onset PD was more prevalet in the non-OH group, with 17 patiets (41.5%), compared to 12 patients (29.3%) in the OH group. Both groups found an equal number of patient (4.3%) in the early onset. Based on the age at onset of motor symptoms, PD can be categorized into juvenile-onset (age < 21 years), earlyonset (≤ 50 years), and late-onset (> 50 years). PD usually occurs in patients between the ages of 55 and65 years, with a prevalence of 1–2% inf people over the age of 60, increasing to approxiamately 3.5% in those aged 85 to 89 years.

The total levodopa equivalent dose (LED) in the OH group was 604 ± 250 mg, which was higher than in the non-OH group (473 ± 217 mg). A previous study also reported that the mean LED was significantly higher in PD patients with OH compared to those without OH. This may be due to the longer disease duration and more severe motor symptoms in the OH group, necessitating higher doses of antiparkinsonian agents. Additionally, the variation in dopaminergic drugs can interfere with autonomic nervous system function, especially because all dopaminergic drugs may influence blood pressure upon standing.[13] Jost *et al.* found no statistically difference (t = 0.91; p = 0.37) in orthostatic blood pressure changes between PD patients taking levodopa and those who didn't, with a comparison of mean values of 45.46 ± 23.76 mmHg vs 43.75 ± 17.88, respectively.[14] Nonetheless, patients with PD who responded well to levodopa tended to exhibit a lower standing mean arterial pressure (MAP) and a greater reduction in blood pressure after taking the medication. Levodopa increased the risk of OH (OR 2.28[95% CI: 0.81–6.46]).[13] The median length of antiparkinsonian agents use was also higher in the OH group compared to the non-OH group: 4.5 years (0.45–15 years) vs 4 years (0–15 years).

Peripherally, levodopa induces vasodilation in the renal blood vessels and inhibits the release of catecholamines from postganglionic sympathetic nerves, reducing sympathetic activity in the smooth muscles of blood vessels and decreasing peripheral vascular resistance. Central hypotensive effects and bradycardia in the brainstem have also been reported in animals. Noack *et al.* reported oral administration of 200 mg of levodopa or 50 mg of benserazide significantly reduced mean arterial pressure (MAP) by 15% ($p < 0.001$), cardiac stroke volume by 13% ($p < 0.01$), and cardiac contractility (dP/dt) by 18% ($p < 0.001$).[15]

Levodopa is a precursor of dopamine and norepinephrine. Peripherally, dopamine decreases vascular resistence (especially in the renal and mesenteric vasculature)and decreases renal sodium transport by activating Gs proteins that are paired with D1-like receptors, which can lead to increased natriuresis and diuresis. At higher concentrations, dopamine increases cardiac inotropy and vasomotor tone directly via α- and β-adrenergic receptors and indirectly via norepinephrine liberation. However, plasma catecholamine (norepinephrine) levels may increase after oral levodopa administration.

Clinically, levodopa-to-dopamine conversion is suppressed by co-medication of peripheral dopamine decarboxylase inhibitors (DDIs), which are aimed to reduce dopamine's peripheral cardiovascular effects. Dopamine is primarily cleared from the synaptic cleft by dopamine transporters. Under conditions of dopaminergic denervation in PD, norepinephrine and serotonin transporters are significantly involved in synaptic dopamine clearance. Increased extracellular dopamine derived from levodopa administration can alter synaptic norepinephrine reuptake, plasma norepinephrine levels, and increase cardiac contractility.[7]

In this study, both the OH group and the non-OH group were mostly comprised of subjects without comorbidities (26.8% vs 24.4%). The comorbid factors identified included dehydration, bleeding, heart failure, tricyclic antidepressant (TCA) use, and history of DM. These result are inconsistent with the previous studies. Dehydration commonly occurs in older people due to reduced thirst response and loss of renal ability to maintain intravascular volume. This can contribute to OH, particulary in cases of decreased stroke volume, a blunted chronotropic response, and impaired vasoconstriction upon standing. In addition, the high prevalence of OH in older people is also influenced by the use of drugs and the underlying disease. OH in older people can occur with or without autonomic nervous system dysfunction. A study by Holmel *et al.* identified comorbidities such as DM, hypertension, and other cardiovascular disease as confounding factor for OH in patients with PD.[8,11] In this study, 63 subjects with PD were diagnosed with OH, among whom 24 subjects (38%) had cardiovascular disease, 9 subjects (14.3%) had DM, 13 subjects (20.6%) had

hypertension, and 22 subjects (34.9%) were using antihypertensive drugs. A study by Li *et al*., reported a significant relationship was found between OH and the presence of DM or increased HbA1c levels in patients with PD.[13] Poor glycemic control, indicated by elevated HbA1c levels, can cause damage to the elasticity of blood vessels, potentialaly leading to OH. Furthermore, insulin resistance and hyperglycemia increase the likelihood of autonomic nervous system dysfunction in diabetics. Denervation of the autonomic system, which can occur simultaneously with endothelial dysfunction and decreased neuropeptide response, further contributes to the development of OH. The use of tricyclic atypical (TCAs) has also been linked to OH. An analysis of three studies involving 261 patients found that TCAs were associated with a significantly higher risk of OH compared to placebo (OR = 6.30; 95% CI: 2.86-13.91) . The ability of TCAs to reduce standing blood pressure is related to their effect on inhibiting sympathetic pathways and reducing vascular retention. Moreover, the use of TCAs in elderly patients may reduce the sensitivity of the baroreflex, further predisposing them to OH.[13] Among antihypertensive medication, CCBs were the most consumed in the OH group (6 subjects; 14.6%), while ACEIs/ARBs were widely consumed in the non-OH group (6 subjects; 14.6%).

After multivariate analysis, this study found that underweight BMI was significantyly associated with OH in PD (p-value = 0.002, OR = 34.571, CI 3.77–317.28). The mechanism underlying the association between underweight BMI and the incidence of OH has not fully understood. One possible mechanism is that increased autonomic activity in patients with high BMI is associated with salt and water retention, which occurs due to activation of the renin-angiotensin-aldosteron system. In contrast, autonomic activity may be reduced in individuals with underweight BMI.[16,17] The autonomic nervous system plays an important role in regulating blood pressure; thus, patients with underweight BMI have greater severity of PD and lower blood pressure on standing or head-up tilt-table testing.[16] Our findings also provide a significant association between BMI and dysautonomia in PD; however, further research is needed to explore whether underweight BMI is a risk factor for OH in PD and wether BMI modification could help prevent OH in this population. The strength of this study lies in the fact that no research has yet addressed OH in Parkinson's disease in the Indonesian population. However, the study's limitations include its small sample size and limited settings (only two hospitals).

## CONCLUSION

Most factors didn't show a significant association with orthostatic hypotension (OH) in Parkinson's Disease (PD) patients, but underweight BMI provided the significant association. Therefore, monitoring and managing OH, along with modifying BMI, are important strategies to prevent complications related to OH.

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**Conflict of Interest**
The authors have no conflict of interests

**Ethic Consideration**
The letter of exemption was issued by Ethics Committee of Dr. Muhammad Hoesin Hospital Palembang on April 27 th, 2023. Certification number: DP.04.03/D.XVIII.6.11/ETIKRSMH/13/2023

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**Author Contributions**
SM, MN, and N collected the data and wrote the manuscript. RN and MHH reviewed and revised the manuscript.

## REFERENCES

1. Kelompok Studi Movement Disorders Perhimpunan Dokter Spesialis Saraf Indonesia. Buku panduan tatalaksana penyakit parkinson dan gangguan gerak lainnya. Syamsudin T, Subagya, Akbar M, editors. Perhimpunan Dokter Spesialis Saraf Indonesia; 2015. [Book]
2. McCann H, Cartwright H, Halliday GM. Neuropathology of α-synuclein propagation and braak hypothesis. *Mov Disord*. 2016; 31(2):152–60. doi: 10.1002/mds.26421
3. Palma J, Gomez-Esteban JC, Norcliffe-Kaufmann L, Martinez J, Tijero B, Berganzo K, et al. Orthostatic hypotension in Parkinson disease: How much you fall or how low you go? *Mov Disord*. 2015; 30(5):639–45. doi: 10.1002/mds.26079
4. Velseboer DC, de Haan RJ, Wieling W, Goldstein DS, de Bie RMA. Prevalence of orthostatic hypotension in Parkinson's disease: A systematic review and meta-analysis. *Parkinsonism Relat Disord*. 2011; 17(10):724–9. doi: 10.1016/j.parkreldis.2011.04.016
5. Bae H-J, Cheon S-M, Kim JW. Orthostatic hypotension in drug-naïve patients with Parkinson's disease. *J Mov Disord*. 2011; 4(1):33–7. doi: 10.14802/jmd.11005
6. Braun M, Amodeo K. Orthostatic hypotension in early Parkinson's disease: A retrospective chart review (2751). *Neurology*. 2021; 96(15_supplement). doi: 10.1212/WNL.96.15_supplement.2751
7. Umehara T, Oka H, Nakahara A, Shiraishi T, Sato T, Matsuno H, et al. Dopaminergic correlates of orthostatic hypotension in de novo Parkinson's disease. *J Parkinsons Dis*. 2021; 11(2):665–73. doi: 10.3233/JPD-202239
8. Farrell MC, Shibao CA. Morbidity and mortality in orthostatic hypotension. *Auton Neurosci*. 2020; 229:102717. doi: 10.1016/j.autneu.2020.102717

9. Mu F, Jiao Q, Du X, Jiang H. Association of orthostatic hypotension with Parkinson's disease: A meta-analysis. *Neurol Sci*. 2020;41(6):1419–26. doi: 10.1007/s10072-020-04277-w
10. Magkas N, Tsioufis C, Thomopoulos C, Dilaveris P, Georgiopoulos G, Sanidas E, et al. Orthostatic hypotension: From pathophysiology to clinical applications and therapeutic considerations. *J Clin Hypertens*. 2019; 21(5):546–54. doi: 10.1111/jch.13521
11. Hommel A, Faber M, Weerkamp N, van Dijk J, Bloem B, Koopmans R. Prevalence and prescribed treatments of orthostatic hypotension in institutionalized patients with Parkinson's disease. *J Park Dis*. 2016; 6(4):805–10. doi: 10.3233/JPD-160853
12. Hiorth YH, Pedersen KF, Dalen I, Tysnes O-B, Alves G. Orthostatic hypotension in Parkinson disease. *Neurology*. 2019; 93(16):e1526–34. doi: 10.1212/WNL.0000000000008314
13. Li L, Guo P, Ding D, Lian T, Zuo L, Du F, et al. Parkinson's disease with orthostatic hypotension: Analyses of clinical characteristics and influencing factors. *Neurol Res*. 2019; 41(8):734–41. doi: 10.1080/01616412.2019.1610224
14. Jost WH, Altmann C, Fiesel T, Becht B, Ringwald S, Hoppe T. Influence of levodopa on orthostatic hypotension in Parkinson's disease. *Neurol Neurochir Pol*. 2020;54(2):200–3. doi: 10.5603/PJNNS.a2020.0019
15. Noack C, Schroeder C, Heusser K, Lipp A. Cardiovascular effects of levodopa in Parkinson's disease. *Parkinsonism Relat Disord*. 2014; 20(8):815–8. doi: 10.1016/j.parkreldis.2014.04.007
16. Nakamura T, Suzuki M, Ueda M, Hirayama M, Katsuno M. Lower body mass index is associated with orthostatic hypotension in Parkinson's disease. *J Neurol Sci*. 2017; 372:14–8. doi: 10.1016/j.jns.2016.11.027
17. Umehara T, Nakahara A, Matsuno H, Toyoda C, Oka H. Body weight and dysautonomia in early Parkinson's disease. *Acta Neurol Scand*. 2017; 135(5):560–7. doi: 10.1111/ane.12633