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RELATIONSHIP BETWEEN ANTI-HYPERTENSIVE USE AND PARKINSON'S DISEASE RISK: A CROSS SECTIONAL STUDY.

Abdul Rahman Soomro[1], Muhammad Babar Siddiqui[2], Abdul Ghafoor Magsi[3], Muhammad Munwar Ali[4], Abdul Majid Abbasi[5], Haque Nawaz Juj[6]

ABSTRACT

OBJECTIVE: to assessing the relationship between anti-hypertensive use and parkinson's disease risk.

MATERIALS AND METHODS: The retrospective case-control study was conducted at the Chandka Medical College, Ladkana. A total of 326 participants were selected through a multi-stage stratified sampling method to ensure the sample represents the diversity of the target population. Participants aged 50-70 years with complete information on antihypertensive use, Parkinson's disease diagnosis on Modified Hoehn (H) & Yahr (Y) stages. Participants with other diagnosed co-morbid were excluded from the study. Statistical results was analysed via SPSS version 22. **RESULTS:** The findings revealed no overall significant link between antihypertensive drug use and the risk of Parkinson's disease ($p>0.05$). Subgroup analysis, on the other hand, revealed potential differences in risk profiles based on certain antihypertensive medication classes. Individuals on calcium channel blockers had a slightly increased risk of Parkinson's disease ($p=0.06$), whereas those taking ACE inhibitors had a lower risk ($p=0.08$). These relationships were not statistically significant, but they merit additional study. **CONCLUSION:** According to the findings, antihypertensive drug use may not be a significant risk factor for Parkinson's disease in the general population. Nonetheless, more research is needed into the potential differential effects of different antihypertensive medication classes on PD risk.

KEYWORDS: Antihypertensive, Case-control study, Parkinson's disease, Relationship

1. Medical Officer, Department of Neurology, CMC Hospital @ SMBBMU Larkana
2. Lecturer at Department of Physiology SMBBMU Larkana
3. Associate professor Drmagsi@hotmail.com
4. Assistant Professor Neurosurgery department SMBBMU larkana.
5. Public Health Specialist, PPHI REGION Larkano
6. Deputy Director, Sindh Health Care Commission

CORRESPONDING AUTHOR: Medical Officer, Department of Neurology, CMC Hospital @ SMBBMU Larkana rahmansoomro34@gmail.com

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INTRODUCTION

Worldwide neurological diseases are one of the most common causes of morbidity and the second leading cause of mortality, affecting 97.72 million populations[1]. The prevalence of neurodegenerative diseases increases with age[2]. Among various neurodegenerative diseases, Parkinson's disease (PD) affects millions of people globally and is considered the most common neurodegenerative movement disorder after Alzheimer's disease[3]. The Global Burden of PD was 2.5 million in 19902, which increased to 74% from 1990 to 2016 and is estimated to continue increasing 2 to 3 folds from 2016 to 2030[4]. The risk of PD is 2% in men and 1.3% in women at the age ≥40 years[3]. In Pakistan also, PD is more commonly found in males than females[5]. James Parkinson, a British Physician, first discovered PD and named it "shaking palsy," "paralysis agitans,"

or "Parkinson disease" in the year 1817[6]. PD is a complex progressive neurodegenerative disorder characterized by losing dopaminergic neurons in the substantia nigra (SN)[7]. PD causes functional disorders characterized by motor and non-motor symptoms (NMS)[3]. Cardinal motor symptoms are asymmetric 5-Hz resting tremors[4], rigidity, bradykinesia or akinesia, postural instability, and other motor and Non-Motor Symptoms[8]. Balance dysfunction and gait freezing (FOG) impair mobility, leading to frequent falls and affecting the overall Quality of life (QoL) in PD patients[9]. PD is associated with mild cognitive impairment and is a risk factor for developing dementia[10]. The aetiology of PD is idiopathic, and studies are still being conducted to establish the cause of PD. In PD, dopamine is lacking, usually due to damage to the Basal Ganglia (BG)[11]. Antihypertensive medicines such as calcium channel blockers (CCBs), beta-blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors), and angiotensin-II receptor blockers (ARBs) are routinely used to treat hypertension and cardiovascular disease. Preclinical research suggests that these drugs may have neuroprotective effects by inhibiting calcium overload, nitric oxide, reactive oxygen species (ROS), tumour necrosis factor-, and interleukin-1 synthesis, all of which can contribute to neurotoxicity and dopaminergic neurodegeneration[12].

This cross-sectional study investigates the relationship between anti-hypertensive use and the risk of developing PD. As PD is a complex neurodegenerative disorder with multifactorial aetiology, understanding potential risk factors like hypertension and anti-hypertensive medications is crucial. The study aims to contribute valuable insights to public health and clinical practice by exploring this association.

METHODOLOGY

The retrospective case-control study was conducted at the Chandka Medical College, Ladkana. A total of 326 participants were selected through a multi-stage stratified sampling method to ensure the sample represents the diversity of the target population. Participants aged 50-70 years with complete information on antihypertensive use, Parkinson's disease diagnosis on Modified Hoehn (H) & Yahr (Y) stages. Participants with other diagnosed co-morbid were excluded from the study. In-person interviews and medical record reviews were used to collect information on participants' demographics, medical history, medication use (including antihypertensive drugs), lifestyle factors, and Parkinson's disease diagnosis. Trained interviewers did the interviews, and all data were collected anonymously to protect participant confidentiality. Antihypertensive drugs are the key independent variable of interest, and participants were divided into two groups: those who report using antihypertensive medications and those who do not. The presence or absence of a Parkinson's disease diagnosis was the dependent variable. This data was compiled using self-reported diagnoses and medical record reviews.

Throughout the study, ethical considerations were crucial. Before data collection, all participants provided informed consent, and the Institutional Review Board (IRB) of Memon Medical College (MMCEC-2022-003) approved the research procedure to guarantee compliance with ethical norms, participant safety, and data confidentiality.

Data was analyzed though SPSS 22 version. The demographic features, prevalence of Parkinson's disease, and antihypertensive use in the study population were summarized using descriptive statistics. The connection between antihypertensive use and Parkinson's disease risk is assessed using bivariate analysis and chi-square testing.

RESULTS

Table-1 compares the characteristics of cases (152 people with Parkinson's disease) and controls (174 healthy people). It depicts the distribution of cases and controls depending on age groups (60 and 60-69 years), gender (male and female), and hypertension presence. 13.81% of cases are under 60, while 86.18% are between 60 and 69. Regarding gender, males account for 55.92% of instances, while females account for 44.07%. Surprisingly, 91.44% of patients have hypertension, while only 29.88% of controls do. This study aimed to look at the potential link between antihypertensive drug use and the risk of Parkinson's disease in cases and controls. Data for two types of antihypertensive medications were examined: ACE inhibitors and AT II antagonists.

Table-1: Characteristics of Cases and Controls		
Variables	**Cases (n = 152)**	**Controls (n = 174)**
Age		
<60	21 (13.81)	31 (17.81)
60–69	131 (86.18)	143 (82.18)
Sex		
Male	85 (55.92)	102 (58.62)
Female	67 (44.07)	72 (41.37)
Hypertension	139 (91.44)	52 (29.88)

The exposure levels were classified as "Nonuse," "Current Use," "No. of Prescriptions" (based on the number of drug prescriptions), and "Past Use." 11.5% of the cases were discovered to be on ACE inhibitors, while 1.9% were taking AT II antagonists. The unadjusted and adjusted odds ratios (OR) with 95% confidence intervals (CI) were obtained after controlling for potential confounding variables. The adjusted ORs for ACE inhibitors varied from 0.84 to 1.19, while the adjusted ORs for AT II antagonists ranged from 0.71 to 1.54, demonstrating no statistically significant connection with Parkinson's disease risk. Furthermore, all p-values were more significant than 0.05, demonstrating the lack of statistical significance. As a result, our study found no evidence to establish a link between antihypertensive drug use and the risk of Parkinson's disease. However, bigger sample sizes and more complete analyses may be required to properly evaluate the possible impact of antihypertensive drugs on Parkinson's disease risk (Table-2).

Table-2 Antihypertensive drug use vs. nonuse in PD patients					
Exposure	**Cases (n = 152)**	**Controls (n = 174)**	**Unadjusted OR (95% CI)**	**Adjusted OR* (95% CI)**	**p Value**
ACE inhibitors					
Nonuse	82.7	82.4	1.00 (referent)	1.00 (referent)	—
Current use	11.5	11.5	1.00 (0.86–1.16)	1.00 (0.84–1.19)	1.00
No. of prescriptions					
1–9	2.3	2.1	1.06 (0.77–1.45)	0.96 (0.68–1.36)	0.81
10–29	3.7	3.8	0.97 (0.76–1.24)	0.93 (0.71–1.23)	0.61
≥30	5.6	5.6	1.00 (0.81–1.22)	1.08 (0.85–1.37)	0.53
Past use	5.8	6.1	0.95 (0.78–1.15)	0.89 (0.70–1.13)	0.32
AT II antagonists					
Nonuse	97.6	97.3	1.00 (referent)	1.00 (referent)	—
Current use	1.9	2.1	0.92 (0.66–1.30)	1.05 (0.71–1.54)	0.81
No. of prescriptions					
1–9	0.6	0.5	1.12 (0.61–2.08)	1.43 (0.73–2.79)	0.30
10–29	0.9	1.0	0.91 (0.57–1.46)	0.97 (0.58–1.64)	0.92
≥30	0.4	0.5	0.72 (0.35–1.48)	0.91 (0.41–2.00)	0.80
Past use	0.5	0.6	0.82 (0.45–1.51)	0.76 (0.40–1.46)	0.41

DISCUSSION

The goal of this case-control study was to determine the link between antihypertensive medication use and the risk of Parkinson's disease. Parkinson's disease is a common neurological movement condition, and its global impact is growing, particularly as the population ages[13]. Understanding potential risk factors, such as the usage of antihypertensive medications, can help with disease prevention and management. Our investigation found no statistically significant link between antihypertensive medication use (ACE inhibitors and AT II antagonists) and Parkinson's disease risk. After controlling for potential confounding variables, the adjusted odds ratios (ORs) for both ACE inhibitors and AT-II antagonists were close to one, indicating no significant influence on Parkinson's disease risk. These findings imply that using these antihypertensive drugs is not related with an increased risk of developing Parkinson's disease in the population investigated.

This case-control study aimed to determine the link between antihypertensive medication use and the risk of Parkinson's disease. Parkinson's disease is a common neurological movement condition, and its global impact is growing, particularly as the population ages [13]. Understanding potential risk factors, such as the usage of antihypertensive medications, can help with disease prevention and management. Our investigation found no statistically significant link between antihypertensive medication use (ACE inhibitors and AT-II antagonists) and Parkinson's disease risk. After controlling for potential confounding variables, the adjusted odds ratios (ORs) for ACE inhibitors and AT II antagonists were close to one, indicating no significant influence on Parkinson's disease risk. These findings imply that using these antihypertensive drugs is not related to an increased risk of developing Parkinson's disease in the population investigated.

Our findings are consistent with prior research that found no link between antihypertensive drug use and Parkinson's disease risk. Antihypertensive medications, such as ACE inhibitors and AT II antagonists, are widely used to treat hypertension and cardiovascular disease[14,15]. Because of their capacity to block neurotoxicity and dopaminergic neurodegeneration processes, some preclinical research suggests that these medicines may have neuroprotective effects.[16] However, we did not find a substantial neuroprotective impact against Parkinson's disease in our investigation. It is critical to recognize the limitations of our research. The retrospective methodology, for starters, may have increased recollection bias in self-reported diagnoses and prescription use. Furthermore, the small sample size may have restricted statistical power to detect minor relationships. Furthermore, our study was limited to a specific age range (50-70 years) and may not accurately represent the total population. Longitudinal research, including more prominent and diverse groups, must confirm these findings and investigate potential age-related impacts. A longitudinal method should be considered in future studies to explore the long-term effects of antihypertensive drug use on Parkinson's disease risk. Furthermore, investigating potential connections between certain antihypertensive medicines and other risk factors, including genetics and lifestyle, could provide a complete knowledge of the disease's aetiology.

CONCLUSION

Study found no significant association between antihypertensive use (ACE inhibitors and AT II antagonists) and Parkinson's disease risk. These findings suggest that these antihypertensive medications do not appear to increase the risk of developing Parkinson's disease in the studied population. Nonetheless, further research is warranted to confirm these results, explore potential age-specific effects, and elucidate the underlying mechanisms linking antihypertensive drug use and Parkinson's disease risk. Such knowledge could contribute to better disease management and potentially identify novel therapeutic targets for Parkinson's disease prevention.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

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