

Correlation of Pupil to Limbus Diameter Ratio with Blood Pressure and Heart Rate among Parkinson's Disease Patients

SAI SAILESH KUMAR GOOTHY¹, ROHIT SINGH CHOUHAN², NAMIT GARG³, ANITA CHOUDHARY⁴, VIJAY KHANDRAO MAHADIK⁵



ABSTRACT

Introduction: Variation in blood pressure and heart rate is observed in patients with Parkinson's disease. Pupil to Limbus Diameter (PDL) ratio is one of the emerging autonomic functions. The studies measuring the autonomic functions of Parkinson's patients are sparse.

Aim: To observe the correlation of the PLD ratio with blood pressure and pulse rate among Parkinson's disease patients.

Materials and Methods: This observational study was conducted among 31 parkinson's disease patients attending Outpatient Ward of General Medicine Department at Ruxmaniben Deepchand Gardi Medical College, Ujjain, Madhya Pradesh, India, from 1st March 2021 to 1st November 2021. Pupil to limbus diameter ratio was recorded using the two-box method. Data was analysed using Statistical Package for Social Sciences (SPSS) version 20.0. Pearson's

correlation was used to observe the correlation. A p-value less than 0.05 was considered significant.

Results: The mean age of the participants was 61.9±13.07 years. The mean PLD ratio of the left eye was 0.343±0.042. There was a significant positive correlation between the PLD ratio of the left and right eye with blood pressure in males. There was a positive correlation between pulse rate also with PLD ratio of the left and right eyes. However, it was not significant.

Conclusion: There was a significant positive correlation of the PLD ratio with blood pressure and pulse rate in males, but negative correlation was observed between the PLD ratio of the left eye with systolic and diastolic blood pressure in females. The study results support the need for further detailed studies in this area to investigate further details of this correlation observed.

Keywords: Autonomic function, Degenerative neurologic disease, Hypertension

INTRODUCTION

Parkinson's disease is a progressive neurodegenerative disease with progressive loss of dopamine secreting neurons in the brain. The symptoms of Parkinson's Disease (PD) include both motor and non motor dysfunctions. Dysfunction of the autonomic system was reported in Parkinson's patients. Autonomic dysfunction is a non motor type of dysfunction [1]. Autonomic functions alteration was reported in the Parkinson's patients along with changes in motor functions. This may be due to damage of the brain areas that are related to regulating the autonomic functions such as the hypothalamus, brain stem, and sympathetic ganglia [2].

One such autonomic dysfunction is pupillometer abnormality due to damage to the ocular autonomic nervous system [3]. Further, there is dysregulation of blood pressure that results in clinical conditions like orthostatic hypotension [4]. Hence, the assessment of autonomic functions of PD patients has prime importance. Pupil to limbus diameter ratio is one of the emerging autonomic function tests that help to assess autonomic activity [5-8]. A positive correlation was observed between the blood pressure and Pupil to Limbus Diameter ratio (PLD ratio) [7,8]. Hence, a hypothesis is considered that there may be a positive correlation between blood pressure and pulse rate with the PLD ratio. This may help for early diagnosis of Parkinson's disease and thus more effective treatment can be offered to the Parkinson's patients. Though the autonomic variations are highly important in Parkinson's patients, the studies related to this area are sparse. Hence, the present study was undertaken to observe the correlation of the PLD ratio with blood pressure and pulse rate in Parkinson's patients.

MATERIALS AND METHODS

The present observational study was conducted at the Department of Physiology, in collaboration with the Department of General Medicine at Ruxmaniben Deepchand Gardi Medical College, Ujjain, Madhya Pradesh, India, from 1st March 2021 to 1st November 2021. The present study was approved by the Institutional Human Ethical committee of R.D. Gardi Medical College (IEC Ref.No-124/2019). Total 31 cases of PD, including both males and females were included in the study by convenient sampling. Patients were recruited from the Outpatient Ward of the General Medicine Department at R.D. Gardi Medical College.

Inclusion criteria: Both male and female participants, aged >18 years and who were in stage 1 and 2 of Hoehn and Yahr classification of disability [9], can ambulate with or without an assistive device for atleast 50 feet, were able to get up and down from the floor with minimal assistance or less and score of 24 or above on the Folstein Mini-Mental State Exam [10] were included in the study.

Exclusion criteria: Participants with age <18 years, with declined immune functions, any other neurodegenerative diseases, eye disorders, and unwilling participants were excluded from the study.

Study Procedure

All the parameters were recorded between 10 am to 11 am to avoid diurnal variation and for the comfort of the participants. Pupil to limbus diameter ratio was recorded using the two-box method explained in the literature [5]. The illumination of the room where the eye pictures were taken was kept constant at 250 lux. After two minutes of rest, the picture of the eyes (left and right) was captured by keeping the light constant in a room in Physiology

Department. The images were captured using sony cyber shot DSC-W800/BCIN5 camera. The captured images were then transferred to the powerpoint slides. Circles were drawn around pupil and limbus manually. Then boxes were drawn to pupil and limbus. The distance between the two ends of the boxes was the diameter of the pupil and limbus respectively [Table/Fig-1]. Then, the ratio of pupil to limbus diameter was calculated. Blood pressure and pulse rate were recorded using HEM 7121 digital blood pressure monitor fully automatic soon after capturing the picture of the eyes.



[Table/Fig-1]: Captured eye pictures and luxmeter; red box is drawn around the limbus and blue box representing the area of pupil.

STATISTICAL ANALYSIS

Data was analysed using Statistical Package for Social Sciences (SPSS) version 20.0. Pearson's correlation was used to observe the correlation. A p-value <0.05 was considered significant.

RESULTS

The mean age of the participants was 61.9±13.07 years. The mean PLD ratio of the left eye was 0.34326±0.042. The mean PLD ratio of the right eye was 0.33768±0.046. The mean pulse rate was 80.94±11.59 beats per minute. The mean systolic and diastolic blood pressure was 138.32±25.74 mmHg and 79.16±12.26 mmHg. There was no significant difference in age, pulse rate, systolic blood pressure, diastolic blood pressure, PLD ratio of left and right eye between males and females [Table/Fig-2].

Parameters	Male (n=25) (Mean±SD)	Female (n=25) (Mean±SD)	p-value
Age (years)	61.92±13.01	61.83±14.57	0.9887
Pulse rate (beats/min)	80.56±12.33	82.50±8.55	0.7194
Systolic blood pressure (mmHg)	140.04±27.41	131.17±17.06	0.4576
Diastolic blood pressure (mmHg)	80.08±13.42	75.33±4.08	0.4037
PLD ratio left eye	0.34756±0.04279	0.32533±0.03625	0.2510
PLD ratio right eye	0.34428±0.04613	0.31017±0.03568	0.1025

[Table/Fig-2]: Comparison of parameters among male and female participants. p-value <0.05 was considered as statistically significant (Student's t-test)

Positive correlation was observed between the PLD ratio of right eye with pulse rate. However, it was not statistically significant. There was significant positive correlation between the PLD ratio of right eye with systolic and diastolic blood pressure [Table/Fig-3]. Positive correlation was observed between the PLD ratio of left eye with pulse rate. However, it was not statistically significant. There was significant positive correlation between the PLD ratio of left eye with systolic and diastolic blood pressure [Table/Fig-4].

There was a significant positive correlation between the PLD ratio of the right eye with Systolic Blood Pressure (SBP) and Diastolic

PLD ratio right eye	Pulse rate (beats/min)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
0.34326±0.042	80.94±11.59	138.32±25.74	79.16±12.26
	r-value=0.0829	r-value=0.5085	r-value=0.5546
	p-value=0.6575	p-value=0.0034*	p-value=0.0012*

[Table/Fig-3]: Correlation of PLD ratio of right eye with pulse rate, systolic and diastolic blood pressure in the study participants.

Pearson's correlation coefficient (Data was presented as mean and SD); *p-value <0.01 was considered as statistically significant

PLD ratio left eye	Pulse rate (beats/min)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
0.33768±0.046	80.94±11.59	138.32±25.74	79.16±12.26
	r-value=0.1386	r-value=0.4856	r-value=0.5453
	p-value=0.4571	p-value=0.0056*	p-value=0.0015*

[Table/Fig-4]: Correlation of PLD ratio of left eye with pulse rate, systolic and diastolic blood pressure in the study participants.

Pearson's correlation coefficient; (Data was presented as mean and SD); *p-value <0.01 was considered as statistically significant

Blood Pressure (DBP) in males. There was a positive correlation between the PLD ratio of the right eye with pulse rate but it was not statistically significant [Table/Fig-5].

PLD ratio right eye	Pulse rate (beats/min)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
0.34428±0.04613	80.56±12.33	140.04±27.41	80.08±13.42
	r-value=0.0772	r-value=0.5052	r-value=0.549
	p-value=0.714	p-value=0.009*	p-value=0.004*

[Table/Fig-5]: Correlation of PLD ratio of right eye with pulse rate, systolic and diastolic blood pressure in male participants.

Pearson's correlation coefficient. (Data was presented as mean and SD); *p-value <0.01 was considered as statistically significant

There was a significant positive correlation between the PLD ratio of the left eye with systolic blood pressure (SBP) and diastolic blood pressure (DBP) in males. There was a positive correlation between the PLD ratio of the left eye with pulse rate but it was not statistically significant [Table/Fig-6].

PLD ratio left eye	Pulse rate (beats/min)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
0.34756±0.04279	80.56±12.33	140.04±27.41	80.08±13.42
	r-value=0.1418	r-value=0.5293	r-value=0.5746
	p-value=0.498	p-value=0.006	p-value=0.002*

[Table/Fig-6]: Correlation of PLD ratio of left eye with pulse rate, systolic and diastolic blood pressure in male participants.

Pearson's correlation coefficient; (Data was presented as mean and SD); *p-value <0.01 was considered as statistically significant

Positive correlation was observed between the PLD ratio of right eye with pulse rate, systolic and diastolic blood pressure in females. However, it was not statistically significant [Table/Fig-7].

PLD ratio right eye	Pulse rate (beats/min)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
0.31017±0.03568	82.50±8.55	131.17±17.06	75.33±4.08
	r-value=0.3858	r-value=0.3955	r-value=0.5734
	p-value=0.450	p-value=0.437	p-value=0.234

[Table/Fig-7]: Correlation of PLD ratio of right eye with pulse rate, systolic and diastolic blood pressure in female participants.

Pearson's correlation coefficient. (Data was presented as mean and SD); *p-value <0.01 was considered as statistically significant

Positive correlation was observed between the PLD ratio of left eye and pulse rate in females. However, it was not statistically significant. Negative correlation was observed between the PLD ratio of left eye with systolic and diastolic blood pressure. However, it was not statistically significant [Table/Fig-8].

PLD ratio left eye	Pulse rate (beats/min)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
0.32533±0.03625	82.50±8.55	131.17±17.06	75.33±4.08
	r-value= 0.282	r-value=-0.0357	r-value=-0.0023
	p-value=0.588	p-value=0.946	p-value=0.996

[Table/Fig-8]: Correlation of PLD ratio of left eye with pulse rate, systolic and diastolic blood pressure in female participants. Pearson's correlation coefficient. (Data was presented as mean and SD); *p-value <0.01 was considered as statistically significant.

DISCUSSION

The present study was undertaken to observe the correlation between the PLD ratio and blood pressure and pulse rate in Parkinson's patients. The mean age of the participants was 61.9±13.07. The mean PLD ratio of the left eye was 0.34326±0.042. The mean PLD ratio of the right eye was 0.33768±0.046. There was no significant difference between the right and left eye PLD ratio. Positive correlation was observed between the PLD ratio of right eye with pulse rate. However, it was not statistically significant. There was significant positive correlation between the PLD ratio of right eye with systolic and diastolic blood pressure. Positive correlation was observed between the PLD ratio of left eye with pulse rate. However, it was not statistically significant. There was significant positive correlation between the PLD ratio of left eye with systolic and diastolic blood pressure.

The dilation and constriction of the pupil are regulated by the autonomic nervous system. Hence, the PLD ratio will be a simple measure for the assessment of the autonomic nervous system. The study results supported the hypothesis that there will be positive correlation in the variables even in Parkinson's patients. Earlier studies also supported the same hypothesis in healthy subjects as well as in females with type 2 diabetes mellitus [6,7]. Similar results were observed in the hypertensive women also [8]. Though earlier studies were of low sample size, they indicated a positive relationship between the PLD ratio and the autonomic functions [6-8]. This is true because both blood pressure and pupil dilation was regulated by the same autonomic system. Sympathetic stimulation raises blood pressure and causes dilation of the pupil whereas parasympathetic stimulation does opposite effects [6,8].

There was no study conducted on the correlation between the autonomic nervous system and the PLD ratio. Hence, the present study was the first study on Parkinson's patients.

There was no significant difference in age between males and females. Pulse rate, systolic blood pressure, diastolic blood pressure, and PLD ratio of left and right eye were not significantly different between males and females. A positive correlation was observed between the PLD ratio of the right eye and pulse rate, systolic and diastolic blood pressure in males. A positive correlation was observed between the PLD ratio of the left eye and pulse rate in males. However, it was not statistically significant. A significant positive correlation was observed between the PLD ratio of the left eye with systolic and diastolic blood pressure in males. A positive correlation was observed between the PLD ratio of the right eye with pulse rate, and systolic and diastolic blood pressure in females. However, it was not statistically significant. A positive correlation was observed between the PLD ratio of the left eye and pulse rate in females. However, it was not statistically significant. A negative correlation was observed between the PLD ratio of the left eye with systolic and diastolic blood pressure. However, it was not statistically significant. The reason for the negative correlation is not clear and has to be assessed in detail in further studies.

The variation in the diameter of the pupil was observed because of alteration of the autonomic activity. Sympathetic stimulation causes dilation of the pupil and parasympathetic stimulation causes constriction of the pupil. Similarly, the variation in blood pressure is also dependent on autonomic activity. Sympathetic stimulation causes an increase in blood pressure and parasympathetic stimulation causes a decrease in blood pressure. Hence, both are controlled by the autonomic nervous system, this may be the reason for the positive correlation observed [7,8]. Change in the blood pressure was reported in PD patients in relation to motor symptoms. As the motor symptoms worsen there is an increase in the blood pressure observed in the PD patients [11]. Due to autonomic dysfunction, multiple daily life functions are affected and there will be a decline in the quality of life of these individuals [12]. It was reported that there was an increased pupillary response in patients with Parkinson's disease [13]. As there is no standard marker for the early diagnosis of Parkinson's disease, the PLD ratio can contribute to the same effectively. It was reported that pupillary response can help in the detection of Parkinson's disease [14].

Limitation(s)

The sample size of the study was less and the study was conducted at single centre. Hence, results cannot be generalised.

CONCLUSION(S)

There was a significant positive correlation was observed between the PLD ratio of the right and left eye with the autonomic functions. In males, a positive correlation was observed between the PLD ratio of right and left eyes with blood pressure and pulse rate. In females, a positive correlation was observed between the PLD ratio of the right eye with blood pressure and pulse rate and the PLD ratio of the left eye and pulse rate. A negative correlation was observed between the PLD ratio of the left eye with systolic and diastolic blood pressure. The study results support the need for further detailed studies in this area to investigate further details of this correlation observed.

REFERENCES

- [1] Chen Z, Li G, Liu J. Autonomic dysfunction in Parkinson's disease: Implications for pathophysiology, diagnosis, and treatment. *Neurobiol Dis.* 2020;134:104700.
- [2] Awerbuch GI, Sandyk R. Autonomic functions in the early stages of Parkinson's disease. *Int J Neurosci.* 1992;64(1-4):07-14.
- [3] Jain S, Siegle GJ, Gu C, Moore CG, Ivanco LS, Studenski S, et al. Pupillary unrest correlates with arousal symptoms and motor signs in Parkinson disease. *Mov Disord.* 2011;26:1344-47.
- [4] Velseboer DC, de Haan RJ, Wieling W, Goldstein DS, de Bie RM. Prevalence of orthostatic hypotension in Parkinson's disease: A systematic review and meta-analysis. *Parkinsonism Relat Disord.* 2011;17(10):724-29.
- [5] Mojumder DK, Patel S, Nugent K, Detoleto J, Kim J, Dar N, et al. Pupil to limbus ratio: Introducing a simple objective measure using two-box method for measuring early anisocoria and progress of pupillary change in the ICU. *J Neurosci Rural Pract.* 2015;6(2):208-15.
- [6] Regi R, Sailesh KS, Mukkadan JK. Pupil to limbus diameter ratio (PlD ratio), olfactory sensitivity and cognition in females with type 2 diabetes mellitus: A case control study. *Research J Pharm Tech.* 2017;10(6):1703-07.
- [7] Sajeevan A, Sailesh KS. Correlation of pupil to limbus diameter ratio (pld ratio) with blood pressure and pulse rate. *Int J Pharm Bio Sci.* 2017;8(3):12-16.
- [8] Archana R, Sailesh KS, Bassetti S, Mishra S. The relationship between blood pressure and pupil to limbus diameter ratio in hypertensive women: A pilot study. *Asian J Pharm Clin Res.* 2017;10(11):142-44.
- [9] Hoehn M, Yahr M. Parkinsonism: Onset, progression, and mortality. *Neurology.* 1967;17(5):427-42.
- [10] Folstein MF, Folstein SE, McHugh PR. Mini-mental status. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189-98.
- [11] Pursiainen V, Korpelainen JT, Haapaniemi TH, Sotaniemi KA, Myllylä VV. Blood pressure and heart rate in parkinsonian patients with and without wearing-off. *Eur J Neurol.* 2007;14(4):373-78.
- [12] Schapira AHV, Chaudhuri KR, Jenner P. Non-motor features of Parkinson disease. *Nat Rev Neurosci.* 2017;18(7):435-50.

- [13] Kahya M, Lyons KE, Pahwa R, Akinwuntan AE, Jianghua HE, Devos H. Pupillary Response to postural demand in Parkinson's disease. *Front Bioeng Biotechnol.* 2021;9:617028.
- [14] Tabashum T, Zaffer A, Yousefzai R, Colletta K, Jost MB, Park Y, et al. Detection of Parkinson's disease through automated pupil tracking of the post-illumination pupillary response. *Front Med.* 2021;8:645293.

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Physiology, Ruxmaniben Deepchand Gardi Medical College, Ujjain, Madhya Pradesh, India.
2. Junior Research Fellow, Department of Physiology, Ruxmaniben Deepchand Gardi Medical College, Ujjain, Madhya Pradesh, India.
3. Associate Professor, Department of Physiology, Ruxmaniben Deepchand Gardi Medical College, Ujjain, Madhya Pradesh, India.
4. Professor and Head, Department of Physiology, Ruxmaniben Deepchand Gardi Medical College, Ujjain, Madhya Pradesh, India.
5. Medical Director, Ruxmaniben Deepchand Gardi Medical College, Ujjain, Madhya Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sai Sailesh Kumar Goothy,
Associate Professor, Department of Physiology, Ruxmaniben Deepchand Gardi
Medical College, Ujjain-456001, Madhya Pradesh, India.
E-mail: dr.saisailesh@gmail.com

PLAGIARISM CHECKING METHODS: [\[Jain H et al.\]](#)

- Plagiarism X-checker: Mar 12, 2022
- Manual Googling: May 02, 2022
- iThenticate Software: Jun 17, 2022 (24%)

ETYMOLOGY: Author Origin**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: Funded by (ICMR-2020-1352). The devices used in this study were provided by Neurovalens (Belfast, UK).
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 03, 2022**Date of Peer Review: **Apr 19, 2022**Date of Acceptance: **May 03, 2022**Date of Publishing: **Jul 01, 2022**