Correlation of pupil to limbus diameter ratio (PLD ratio) with blood pressure and pulse rate in hypertensive males

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**ABSTRACT**

Hypertension is known to be a major risk factor for coronary artery disease, stroke, heart failure, vision loss which remains asymptomatic until late in its course and even severely elevated pressures can be clinically silent for years. Measurement of diameter of the pupil is indicative of autonomic function, and recording of the pupil to limbus diameter (PLD) ratio correlates with alterations in blood pressure. As hypertension is more prevalent in males and the incidence is increasing year by year, measurement of PLD ratio can be used as a simple screening tool in the general population to measure the autonomic alterations associated with changes in blood pressure. This study aims at finding the correlation of pupil to limbus diameter (PLD) ratio with blood pressure and pulse rate in Hypertensive Males. 45 male patients attending O/P of Saveetha Medical College and Hospital in the age group of 30 to 65 years, fulfilling the inclusion criteria were enrolled in the study. It's a case-control study with non-probability convenient sampling. Blood pressure, using a sphygmomanometer and pulse rate were measured by the physician according to AHA criteria, and PLD ratio was assessed by the two-box method. There was a significant decrease observed in PLD ratio when normal and hypertensive groups. Mean pulse rate of hypertensive males was significantly higher compared to the control group. The systolic blood pressure and diastolic blood pressure were significantly high in hypertensive male patients. A significant difference in PLD ratio exists between the control and hypertensive males though no positive correlation was observed.

**Keywords:**
Autonomic function test, Blood pressure, Hypertension, Pulse rate, Pupil to limbus diameter ratio (PLD ratio)

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INTRODUCTION

Globally, hypertension is considered to be a major cause of premature death, according to the World Health Organization (WHO). (Mackay J et al., 2004). The prevalence of hypertension is 25% in urban and 10% in rural India. Hypertension is the cause for 57% of the deaths due to stroke and 24% of the deaths due to coronary heart disease. (Gupta R, 2004). WHO has estimated the prevalence of elevated blood pressure in men to be 32.5% and women to be 31.7% in India (no communicable diseases country profiles, 2011). Hypertension is known to be a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease and dementia. Unfortunately, hypertension typically remains asymptomatic until late in its course and even severely elevated pressures can be clinically silent for years. (Robbins and Cotran, 2015). In a multi-centric study among the elderly in India, it was found that only 25.6% of patients undertaking the drugs for
hypertension had their blood pressure (BP) under control. (Hypertension study group, 2001). Thus the control of hypertension is inadequate, and the majority of cases remain undetected. (Mohan V et al, 2007). Therefore, regular monitoring of BP and early diagnosis of hypertension will go a long way in saving lives. (Gulec S, 2013).

Measurement of diameter of the pupil is indicative of autonomic functions, and recording of the pupil to limbus diameter (PLD) ratio correlates with alterations in blood pressure in women. (Archana R et al, 2017). PLD ratio is defined as "the ratio of the pupillary diameter measured at an axial plane with the limbal diameter measured at a same or parallel axial plane". (DK Mojumder et al, 2015). The pupil is an aperture, located in the centre of the iris of the eye and plays a key role in regulating the entry of light into the retina. The amount of light that enters the eye through the pupil is proportional to the area of the pupil or to the square of the diameter of the pupil. The limbus is the border between the opaque white sclera and the transparent cornea. The muscles that regulate pupillary size are the circumferential sphincter muscle, which is innervated by the parasympathetic nervous system and the iris dilator muscle, which is innervated by the sympathetic nervous system. The activation of the sphincter muscle, under parasympathetic control, constricts the pupil (miosis) whereas activation of the dilator, under sympathetic control dilates the pupil (mydriasis). The pupil dilates through sympathetic stimulation by the release of adrenaline and by parasympathetic inhibition. (Aruna S et al, 2017; Guyton et al, 2016). In hypertensive working women, a positive correlation between PLD ratio of right and left eye with blood pressure was observed. (Archana R et al, 2017).

Though many autonomic function tests exist like a cold pressor test, Valsalva manoeuvre, isometric handgrip test, head-up tilt test and analysis of heart rate variability, not a single, rapid, simple to administer test exists which can correlate with changes in BP in hypertensive patients. Thus this study was aimed at the correlation of pupil to limbus diameter (PLD) ratio with blood pressure and pulse rate.

There was an evaluation of blood pressure, pulse rate and pupil to limbus diameter ratio (PLD ratio) by standard and two-box method and hence an assessment on the relation of the pupil to limbus diameter ratio with blood pressure and pulse rate in normal and hypertensive males performed.

MATERIALS AND METHODS

The study was conducted after obtaining permission from the Institutional Ethics Committee (IEC) of Saveetha Medical College and Hospital. This is a case-control study conducted on patients attending O/P of Saveetha Medical College Hospital. A total number of 90 male participants in the age group of 30 to 65 years were included in the study. It is a non-probability convenient sampling where willing male patients of age 35 to 60 years with primary hypertension without any comorbid illness and any complications were included. All unwilling male patients and those with a comorbid illness like diabetes, thyroid, cardiac disease, asthma and renal disease were excluded from the study.

Among the participants, 45 were a control group with normal blood pressure, and 45 belonged to hypertensive group fulfilling the inclusion criteria. Written informed consent was obtained from study participants. Strict confidentiality was maintained regarding all the information obtained from the patient. All the subjects were screened by taking a medical history and the demographic details of the patients like age, sex; weight was recorded. The clinical examination was performed by a qualified physician.

The assessment of blood pressure, pulse rate and PLD ratio was performed at 1.00 pm for the convenience of the participants and to overcome the effect of diurnal variation. The patients were assigned to the hypertension group after screening by the qualified, experienced physician.

Measurement of blood pressure (BP)

Was performed according to AHA 2017 criteria. (American Heart Association, 2017). Blood pressure and pulse rate were recorded using fully automatic M60 diamond digital blood pressure monitor (Industrial Electronic and allied products) from the right hand. The participants were seated in a chair and allowed to relax, (feet on the floor, back supported) for about 5 mins. It was made sure that the participants avoided caffeine, exercise and smoking for at least 30 min before the measurement. Participant’s arm was supported appropriately (e.g. resting an arm on a desk) and by using the correct cuff size, middle of the cuff was positioned on participant’s upper arm at the midpoint of the sternum. At first visit, BP in both arms was recorded, and arm with higher reading was used. Palpated estimation of radial pulse obliterated pressure for systolic BP was used, and the cuff was inflated 20-30 mmHg above the level obtained to determine the BP level. The cuff was deflated at pressure 2 mmHg per second, and
Korotkoff sounds were heard. Systolic BP was recorded at the onset of 1st Korotkoff sound and diastolic BP at the disappearance of all Korotkoff sounds, using the nearest even number. For estimation of the individual’s BP level, 3 readings were taken, and the lowest value obtained was used. (American Heart Association, 2017).

**Measurement of pulse rate**

The participants were seated comfortably in a chair and allowed to relax. It was made sure that participant did not walk, climb stairs or otherwise exert himself in the last 20 minutes. Tips of physician’s first, second and third finger were pressed gently on inside of the participant’s wrist. The pulse rate was measured and recorded for one complete minute. (Dianne P, 2013).

**Measurement of the pupil to limbus diameter (PLD) ratio**

![Image of eye with measurement boxes](image)

**Figure 1: Measurement of PLD ratio**

Limbus diameter (A, blue line) = 3.68 cm; Pupil diameter (B, orange line) = 1.43 cm; Pupil to limbus ratio = 0.389

**PLD ratio:** The PLD ratio is defined as the ratio of pupillary diameter measured at the parahorizontal axial plane with that of the limbus diameter measured at the same or parallel axial plane. PLD ratio was measured by the two-box method as described in the literature. (DK Mojumder et al., 2015).

**Image capture:** Before capturing the image of the eye, the participants were exposed to ambient light levels for at least 5 minutes. Background illumination was measured and kept constant of 163 lux at the eye level of the participant in a sitting position. Illuminance measurement of ambient light conditions was made using Luxmeter (Model no. MTQ 1010A, Metro Q) with a range of 0-20,000 Lux and resolution of 1-100 Lux and repeatability ± 2%.

The camera of a cell phone (Samsung) with built-in spot metering capability and autofocus capability was used. This is for the reflectance of light from the patient’s iris/pupillary area to automatically adjust for exposure without the use of flash. Upon directing the camera towards the patient’s eyes, the region of interest (iris/pupil) was focused and photographed.

**Image analysis:** All images were adjusted for brightness and contrast for a clear demarcation of pupillary margins. Microsoft office PowerPoint 2010 was used to measure PLD ratios. The PLD ratio was estimated by a two-box method. Two boxes were drawn using the rectangular tool of the drawing toolbar, such that the heights of the two boxes are equal and superimposed. The widths of the boxes were adjusted manually so that its width represents the limbal and the pupillary diameters respectively. For each PLD ratio, limbus and pupillary diameters were estimated in the same or parallel axial plane. (DK Mojumder et al., 2015).

**Statistical analysis:** Data was analysed by SPSS 20.0. The student T-test was applied between the normal and the hypertensive group to assess the significant difference between the SBP, DBP, PLD and PR between the study and the control group. Pearson correlation coefficient and regression analysis were used to assess the relation of the pupil to limbus diameter ratio with blood pressure and pulse rate in normal and hypertensive male patients. p<0.05 was considered as significant.

**RESULTS**

**Table 1: Mean ± SD of age, PLD ratio, pulse rate, SBP & DBP in the study group (hypertensive group) and control group (normal group)**

| Parameters | Control Group (n=45) | Study Group (n=45) |
|------------|----------------------|--------------------|
| Age        | 45.12±5.21           | 42.93±7.78         |
| PLD ratio  | 0.37±0.03            | 0.35±0.04**        |
| PR         | 67.02±4.52           | 76.76±1.45***      |
| SBP        | 108.98±8.37          | 135.82±10.21***    |
| DBP        | 72.58±7.11           | 89.47±8.26***      |

**Figure 2: Comparison of PLD between control and study group (hypertensive group)**
Data from 45 normal and 45 hypertensive male participants were analyzed. Table 1 presents the comparison of mean ± SD (standard deviation) value of age, PLD ratio, pulse rate (PR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) parameters of the normal control group and hypertensive study group using T-test. Age was not significantly different among the control and hypertensive group.

The mean PLD ratio of both left and right eyes was taken. There was a significant decrease observed in PLD ratio when normal and hypertensive groups were compared (p<0.01, figure 2). Mean pulse rate of hypertensive males was significantly higher compared to the control group (p<0.001, figure 3). The systolic blood pressure and diastolic blood pressure were significantly high in hypertensive male patients (p<0.001, figure 4).

No significant correlation was observed between SBP and PLD ($R^2 = 0.614$, $p < 0.101$, figure 5) as well as between DBP and PLD ($R^2 = 0.0707$, $p < 0.078$, figure 6). Correlation between PR and PLD was also not significant ($R^2 = 0.0017$, $p < 0.786$, figure 7). No significant correlation was observed between SBP and PLD ($R^2 = 0.0491$, $p < 0.101$, figure 8) as well as between DBP and PLD ($R^2 = 0.002$, $p < 0.078$, figure 9). Correlation between PR
and PLD was also not significant ($R^2 = 0.003$, $p < 0.786$, figure 10).

Figure 10: Correlation between PR and PLD in the control group

DISCUSSION

In the 1.2 billion Indian populations, the prevalence of hypertension was estimated at 3% to 34.5% in males and 5.8% to 33.5% in females. (Das SK et al., 2005; WHO 2010). Over the last sixty years, a steady increase in the prevalence of hypertension has been observed. A significantly higher risk was observed in an urban population from 2% to 25% than in rural residents, where it increased from 2% to 15%. The prevalence increases with age in all the populations. (MK Singh et al., 2016). In India, 57% of stroke deaths and 24% of coronary heart disease deaths are due to hypertension. (Gupta R, 2004). Presence of hypertension is known to increase the risk of developing cardiovascular diseases, cerebrovascular diseases, and chronic kidney diseases. (Wu S et al., 2013; Huang Y et al., 2013; Kim MJ, 2012). This alarming trend has highlighted hypertension as an emerging public health problem and is called a silent killer disease. (Venkataraman R et al., 2013; Dhianawaty DD et al., 2017).

The pupil of the eye is located in the centre of the eye and is responsible for regulating the light entry. It responds immediately to lighting changes in the surrounding environment by constriction or dilation according to the current need, thereby always allowing optimum light entry. (Oyster CW, 1999; Beatty J et al., 2000). Variations in the pupil diameter are regulated by two muscles, the sphincter and dilator which are innervated by the parasympathetic nervous system and sympathetic nervous system simultaneously. (Walker HK et al., 1990). Sympathetic stimulation causes the pupil to dilate by the release of adrenaline, while parasympathetic inhibition also occurs. (Bradley MM et al., 2008; Fotiou F et al., 2000).

Recent studies show that there is a positive correlation between blood pressure and PLD ratio and a strong correlation between PLD ratio and pulse rate in healthy women. (Archana R et al., 2017). In this study, a significant difference was observed between the PLD ratio of normotensive and hypertensive men though there was no correlation between PLD ratio with BP and pulse rate. The sympathetic nervous system helps in the regulation of blood pressure (Philip Thomas et al., 2015) and mediates the development and maintenance of hypertension. (Avisha Singla et al., 2015). In a hypertensive patient, there is an autonomic dysfunction leading to sympathetic overactivity; hence, the excessive adrenergic stimulus is produced. (Stevo Juliusn, 2018). Apart from this, parasympathetic inhibition also occurs, leading to sustained hypertensive state. Physiologically, the pupil dilates through sympathetic stimulation by the release of adrenaline and by parasympathetic inhibition. (Aruna Set et al., 2017; Guyton et al., 2016). In this study, there was a significant difference in PLD ratio exists between the control and hypertensive males though no positive correlation was observed. As both pupil diameter and blood pressure are influenced by the sympathetic and parasympathetic nervous system, the observed difference in PLD ratio may be due to this fact.

CONCLUSION

All the existing autonomic function tests are time-consuming and require expertise in administration. In comparison with the other tests, the PLD ratio is easily measurable, less time consuming and cost effective. This study will throw new light on using pupil to limbus diameter (PLD) ratio as a simple non-invasive procedure to assess the autonomic function alterations associated with changes in blood pressure. As hypertension is more prevalent in males, and the incidence is increasing year by year, measurement of PLD ratio can be used as a simple screening tool in the general population to measure and analysis of heart rate variability not a single, rapid, simple to administer test exists which can correlate with changes in BP in hypertensive patients.

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