

Correlation between Central Corneal Thickness Corrected Intraocular Pressure with Systolic Hypertension in Adults Over 40 Years in a Tertiary Eye Care Centre

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ABSTRACT

BACKGROUND

Glaucoma is a chronic, progressive optic neuropathy leading to irreversible blindness. Raised intraocular pressure is one of the modifiable risk factors of developing glaucoma. Regulation of intraocular pressure (IOP) is influenced by various factors and, systolic hypertension is one of them. The objectives of the study was to assess the relationship between systolic hypertension and IOP, also to see the effect of controlled and uncontrolled systolic blood pressure (SBP) on IOP in adults above 40 years of age.

METHODS

This study included a total of 230 known systemic hypertensive patients of age above 40 years. All the patients underwent detailed history taking, careful systemic and ocular examination. IOP was measured by Goldmann applanation tonometer, central corneal thickness (CCT) by anterior segment optical coherence tomography (OCT) and blood pressure (BP) was recorded after 5 minutes of rest. The data was recorded.

RESULTS

Correlation coefficient for SBP and IOP in right eye (RE) was 0.290 and for left eye (LE) was 0.354 with a probability value of $P < 0.0001$ which was statistically highly significant. Mean IOP for controlled SBP was 17.76 mmHg in both eyes (BE) which increased to 20.19 mmHg in RE and 20.64 mmHg in LE in uncontrolled SBP. The Z score value between controlled and uncontrolled systolic hypertensive patients in RE and LE was 6.11 and 7.06 respectively ($P < 0.0001$). There was an increment of IOP for every 10 mmHg in SBP by 0.56 mmHg in right eye and 0.73 mmHg in left eye.

CONCLUSIONS

Systolic blood pressure is significantly correlated with IOP. The uncontrolled SBP was related to higher mean IOP and mean IOP was found to increase with rise in SBP. Therefore, patients with known hypertension and glaucoma have to be regularly followed-up and should keep their BP in normal range to prevent disease progression.

KEYWORDS

Intraocular Pressure, Central Corneal Thickness, Systolic Blood Pressure, Adults Above 40 Years

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BACKGROUND

Human eye is a fluid filled spheroid having flexible and partially elastic wall. Maintenance of a stable shape is necessary for optical properties of the eye and is maintained within a fairly narrow range by intraocular pressure (IOP).¹ Regulation of IOP is a complex physiological mechanism that depends on the production of aqueous humour, resistance to aqueous humour outflow and episcleral venous pressure.² The mean IOP value in the general population is approximately 16 mmHg $\pm$ 2 SDs to either side of the mean, and range of roughly 10 to 21 mmHg². From clinical point of view, IOP is one of the major risk factors for glaucoma.^{3,4} Glaucoma is not a single disease, but a group of ocular conditions which differs in their clinical manifestation, pathophysiology and management. These ocular conditions have certain similar features like optic disc cupping, retinal ganglion cell loss associated with characteristic visual field loss and most of the time related to the level of intraocular pressure.

Therefore, glaucoma is defined as disturbance of the structural or functional integrity of optic nerve that can usually be arrested or diminished by adequate lowering of IOP.⁵

The World Health Organization regards glaucoma as the second largest cause of bilateral blindness after cataract and it causes irreversible blindness. It was estimated that 60.5 million people would be affected by glaucoma, both primary open-angle and primary angle-closure glaucoma globally in 2010. It is likely to be 76 million by the year 2020 and expected to affect 111.8 million people by 2040.⁶

Small variation in either rate of production or in the rate of outflow of aqueous humour from the eye can result in large changes in IOP. Despite relative constancy of IOP, there are various factors that contribute to variation of IOP. Intraocular pressure is influenced by race, age, sex, refractive error, systemic disease, trauma and family history etc. Common systemic parameters which affect the IOP are hypertension, diabetes mellitus, obesity, body mass index, cardiovascular parameters and Graves' disease.⁷ These systemic parameters represent clinically modifiable risk factors, which might provide certain new treatment modalities beyond IOP reduction in glaucoma treatment.

Increased blood pressure (BP) has been thought to cause raised IOP by elevating ciliary artery pressure and consequently an increase in production of aqueous humour.⁸ Bill et al. demonstrated that variations in SBP resulted in small changes in aqueous humour formation, possibly related to increased capillary pressure in the ciliary body.⁹ It can also affect IOP by change in sympathetic tone, atherosclerotic changes and high levels of renin-angiotensin. All these factors can affect the pressure of epi-scleral vein which regulates the aqueous humour outflow through the Schlemm's canal, which in turn affects the IOP.¹⁰

IOP has been found to have a significant relationship with central corneal thickness (CCT).¹¹ Thin corneas lead to an underestimation, and thick corneas lead to an overestimation of IOP. The effect of SBP on IOP is complex and CCT is significant to get more accurate IOP. Therefore, in present study we wanted to investigate the

interrelationship of CCT corrected IOP with systolic blood pressure in adults, also to see the effect of well controlled and uncontrolled SPB on IOP and importance of regular follow-up of these patients to prevent disease progression.

METHODS

It was an observational cross-sectional study, which was carried out in the ophthalmology department over a period of 1 year from February 2017 to January 2018 after taking due permission from the institutional ethical committee. A total 230 patients with a history of systemic hypertension above 40 years of age were enrolled in this study, who were attending the OPD of the institute. Before enrolment; informed written consent was obtained from each of the patients.

Systolic blood pressures $\geq$ 140 mmHg, diastolic blood pressure $\geq$ 90 mmHg or persons taking antihypertensive medications were defined as hypertensive.¹² Patients between 40 - 80 years of age, either sex, known case of hypertension with or without treatment were included in this study.

Exclusion Criteria

Patients with established inflammatory, degenerative, traumatic pathology of eye or any intraocular surgery, any known systemic disease other than hypertension and any type of diagnosed glaucoma cases, as well as patients not willing to participate in study were excluded.

A detailed personal history was taken from all the patients that included name, age, gender, occupation, any chronic illness and medication. Then, all the participants underwent a comprehensive ocular and systemic examination. The ocular examination included measurement of visual acuity; the detailed examination of the anterior segment was done by using standard technique and equipment. Posterior segment examination was done by + 90 D lens on slit-lamp biomicroscope or indirect ophthalmoscope after dilation of pupil. Intraocular pressure measurement was done by Goldmann applanation tonometer. Intraocular pressure was recorded during 10am to 12 noon to avoid any effect of diurnal variation in the reading. Gonioscopy was done in all the patients to assess the anterior chamber angle. CCT measurements were obtained from each eye with a radial anterior segment mode in TOPCON: 3 D OCT-1 Maestro version 8.3 X., then IOP was adjusted according to CCT reading as per the modified Ehlers correction factor algorithm.¹³

Blood pressure of participants was measured with a sphygmomanometer after 5 minutes of rest. Recordings of BP were graded as controlled or uncontrolled hypertensive as per optimal target blood pressures during antihypertensive treatment: BHS (British Hypertension Society) Guidelines.¹² Patient's detailed medical history about hypertension, diabetes and any other systemic illness or any past intraocular surgery was obtained by using the interview questionnaire.

Statistical Analysis

The data was presented as mean $\pm$ SD or patient's number and percentage. Statistical analysis of data was performed using z test, Pearson's correlation coefficient and linear regression coefficient wherever appropriate. The null hypothesis was rejected for P value < 0.05 .

RESULTS

During the entire study period, a total of 230 patients were included for the study after they gave informed written consent and fulfilled the inclusion criteria.

Table 1 shows socio-demographic data, out of total 230 patients there were 118 (51 %) males and 112 (49 %) females in this study. The participants included in this study were in the age range of 40 - 80 years, and mean age was of 52 (± 8.2) years. To see age wise distribution, patients were divided into 5 groups with increasing age at the interval of 10 years and found the most common age group was between 40 - 50 years which accounted for 50 % (115) of the patients. While 71 - 80 years age group had least frequency 2.17 % (5).

All patients were diagnosed with systemic hypertension and among them 139 (60.43 %) patients were diagnosed with disease up to 5 years, only 9 (3.9 %) had history of hypertension more than 15 years.

145 (63 %) patients out of 230 had their SBP under control and 85 (37 %) patients had uncontrolled SBP at the time of presentation and the range of controlled or uncontrolled SBP was decided on the basis of British Hypertension Society guidelines for optimal target of BP during antihypertensive treatment.

Data obtained showed the mean IOP of right eye to be 17 (± 3.85) mm Hg and in left eye was also 17 (± 3.80) mm Hg. Mean CCT in right eye was 525 (± 28.58) μ m as against 524 (± 28.76) μ m in left eye. Mean CCT corrected IOP in right and left eye was 18 (± 4.11) mmHg and 18 (± 4.12) mm Hg respectively.

Correlational analysis for the relationship between CCT and IOP was $r_{RE} = 0.145$ and $r_{LE} = 0.131$ with $P = 0.0272$ and $P = 0.0462$ respectively in RE and LE, which was considered to be weakly statistically significant. To find out correlation between SBP and IOP the Pearson's correlation coefficient was analysed in RE and LE which came out to be 0.29 and 0.34 respectively. The two-tailed P value for RE and LE was less than 0.0001 and this difference by conventional criteria were considered to be highly statistically significant.

Mean IOP in patients with controlled SPB was 17.76 mmHg and uncontrolled SPB was 20.41 mmHg. Then z-score was calculated between controlled and uncontrolled systolic hypertensive in RE and LE was 6.11 and 7.06 respectively, P-value was < 0.0001 and according to conventional criteria, this difference was considered being statistically highly significant.

Table 2 shows effect of increasing range of SBP on IOP, for this we divided the patients into 5 groups with increasing range of SBP at the interval of 20 mmHg from 100 mmHg to more than 180 mmHg. Mean IOP for all ranges was calculated, regression coefficient analysis was done to assess the relationship of IOP with SPB. Here systolic blood pressure was taken as independent variable and IOP as dependent variable, the relationship of SBP and IOP came out statistically significant (< 0.00001).

Table 3 shows the correlation of IOP with systolic blood pressure. According to correlation analysis study, prediction of subject's IOP from their SPB could be done by using the formulae: IOP in mmHg = $11.09 + 0.056$ (SBP) and $9.076 + 0.073$ (SPB) for right eye and left eye respectively.

Figures 1 and 2 shows the linear rise of IOP with increasing SPB in right eye and left eye respectively. Here we found that for every 10 mmHg rise in SBP, IOP was increased in RE by 0.56 mmHg and LE increases by 0.73 mmHg. So, on regression analysis we found that there was significant impact of SBP on IOP

Variables		Numbers (N)	Percentages (%)
Mean Age in Years (Mean $\pm$ SD)		52 (± 8.2) years	
Gender	Male	118	51
	Female	112	49
Age wise distribution	40 - 50 years	115	50
	51 - 60 years	78	33.91
	61 - 70 years	32	13.91
	71 - 80 years	5	2.17
Duration of hypertension (in year)	1 - 5	139	60.43
	6 - 10	63	27.39
	11 - 15	19	8.2
	More than 15	9	3.9
Hypertension status	Controlled	145	63
	Uncontrolled	85	37

Table 1. Socio-Demographic Characteristics of the Study Population (N = 230)

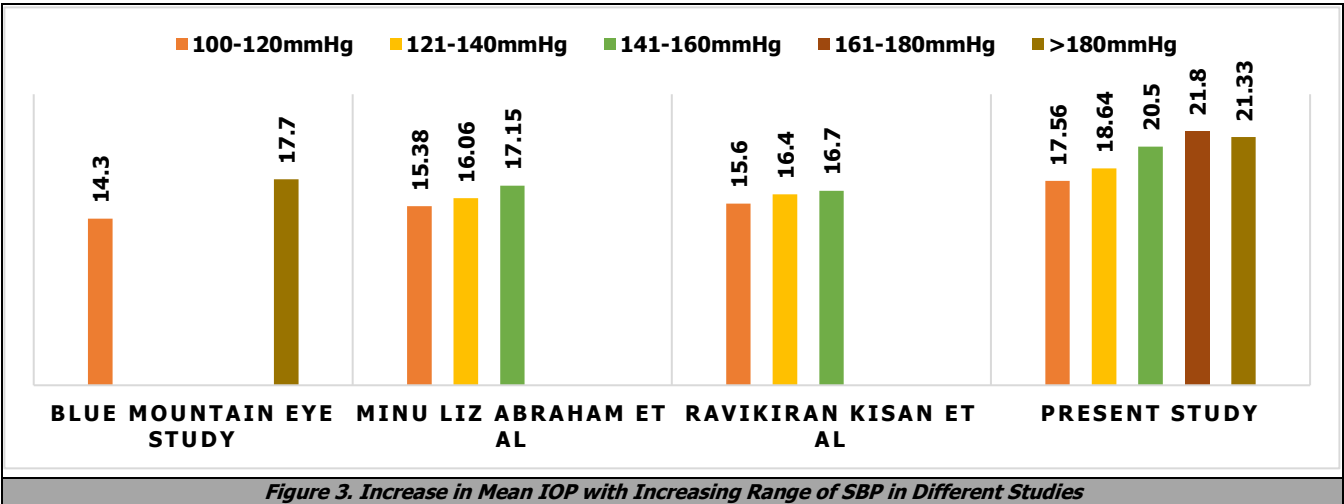
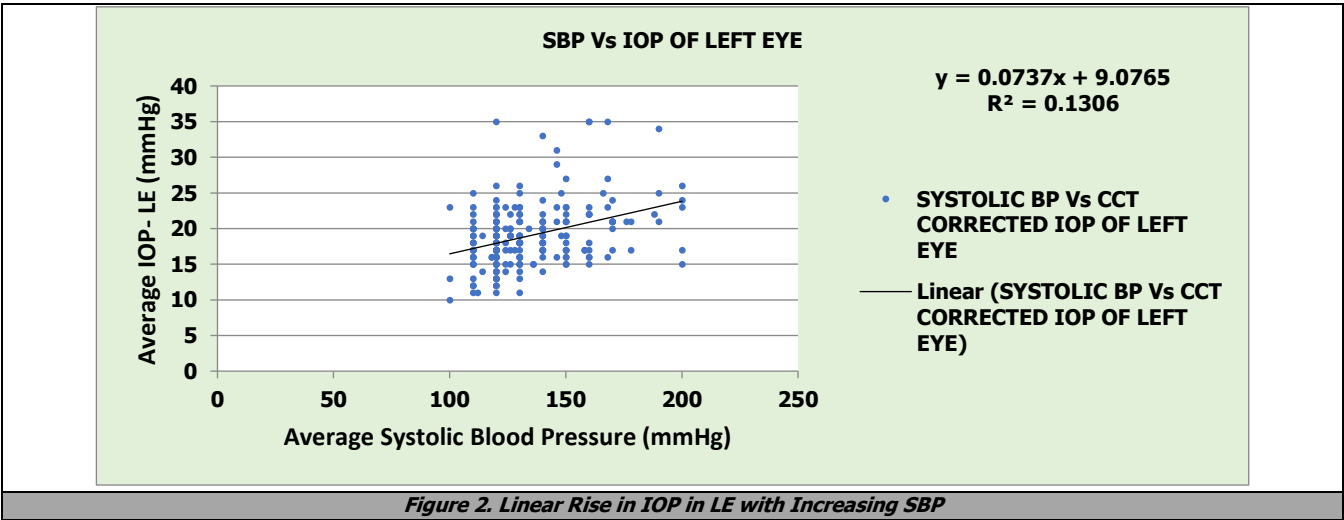
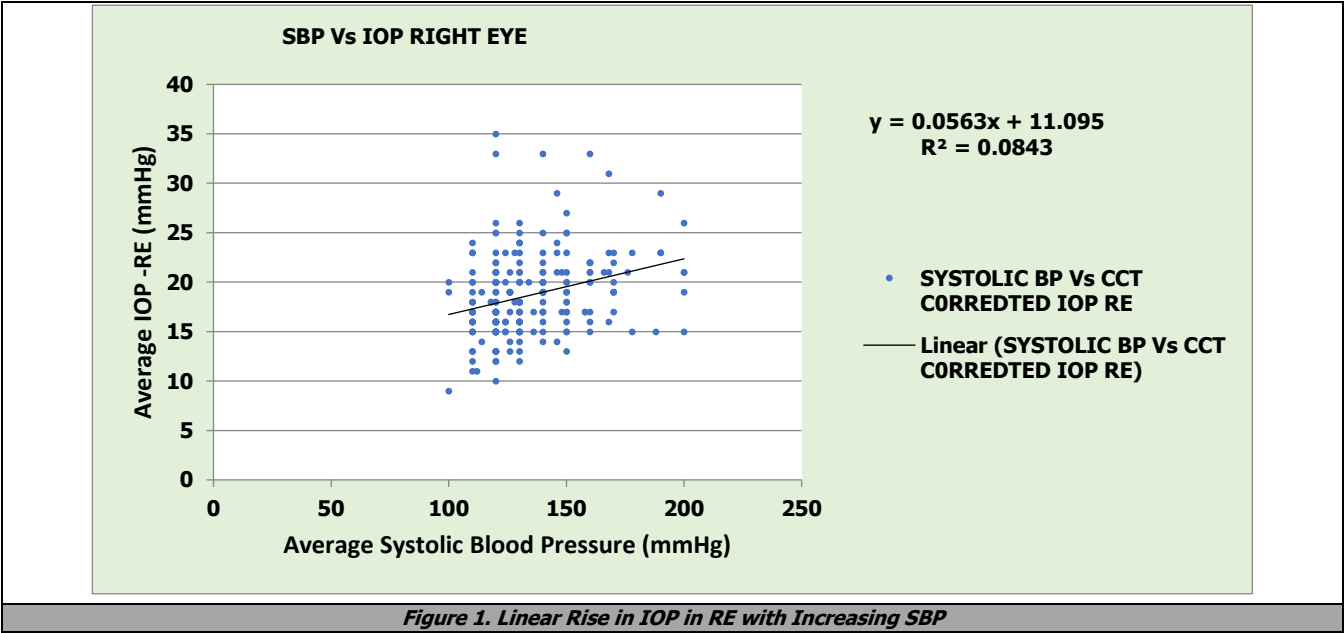
Range of SBP (mmHg)	Mean IOP RE (mmHg)	Mean IOP LE (mmHg)
100 - 120	17.56 $\pm$ 4.20	17.45 $\pm$ 3.08
121 - 140	18.58 $\pm$ 3.4	18.64 $\pm$ 3.21
141 - 160	20 $\pm$ 4.21	20.5 $\pm$ 5.10
161 - 180	21.07 $\pm$ 3.4	21.8 $\pm$ 3.74
More than 180	21.33 $\pm$ 4.3	21.33 $\pm$ 4.01

Table 2. Range of SBP and Mean IOP

Relationship of IOP with SBP	Correlation Coefficient	P Value	Regression Coefficient (R Coefficient)	95 % CI	IOP Estimation in mmHg
Right eye	+ 0.29	$< 0.0001^*$	0.056	0.03 to 0.08	IOP = $11.09 + 0.056$ (SBP)
Left eye	+ 0.34	$< 0.0001^*$	0.073	0.04 to 0.09	IOP = $9.076 + 0.073$ (SPB)

Table 3. Correlation of IOP with SBP

*indicates statistical significance at $P < 0.05$



DISCUSSION

Increased SBP and IOP may have adverse effects if left untreated and so these parameters should always be

examined in patients whenever they visit eye care professionals. Therefore, in our study we have investigated possible relationship between SBP and IOP, but the knowledge of this interrelationship is not yet completely understood. As, IOP is regarded as one of the most

important modifiable risk factors which is associated with development and progression of glaucomatous optic atrophy, therefore factors that influence IOP and its measurement is of great relevance in understanding the pathogenesis of diseases and reducing the burden of blindness.

Present study included a total of 230 patients, average age was 52 ($\pm$ 8.2) years and age range was between 40 - 80 years. The most common age group was in 40 - 50 years representing 50 % of the total study population. Similar demographic distribution was seen in study done by Mansoor Ud Din et al.,¹⁴ while Samuel Hodor et al.¹⁵ study 50 - 59 years was the most common age group.

The likelihood of hypertension increases with age, earlier studies have reported prevalence of hypertension as 55 % among 40 - 60 years age group during 2000.¹⁶ With increasing age, progressive constriction takes place in homeostatic reserve and this change is defined as homeostatic stenosis. This usually starts by 3rd decade of life and gradually progresses with age, and manifest in eye and cardiovascular system as changes in IOP and BP. This justifies why 40 - 50 years age group is most common in this present study.

In Baisakhi S, et al.¹⁷ study, mean IOP of hypertensive group was 17.93 $\pm$ 2.22 mm of Hg. Similar result was seen in present study also. Here mean IOP of patients diagnosed as case of systolic hypertension was 18 ($\pm$ 4.11) mmHg and 18 ($\pm$ 4.12) mmHg in right and left eye respectively. This is also comparable to the study conducted by SD McLeod et al.¹⁸ where they found middle aged male patients with higher systolic blood pressure had higher IOP than age matched control.

Mean central corneal thickness in present study, measured by OCT in radial anterior segment mode was 525 μ m in RE and 524 μ m in LE. Our study was comparable to mean CCT value using AS - OCT in the study done by Badran T et al.¹⁹ and Kamath M et al.¹¹ They also found that there was around 0.9 mmHg increase in IOP for every 10 microns increase in CCT.

As we had taken CCT into account in our study to get accurate IOP, we also saw correlation between CCT and IOP which was statistically significant and such correlation has been established in other studies too like LALES,²⁰ study done by Kamath M et al.,¹¹ Gelaw Y et al.²¹

Hennis et al.⁸ study concluded that increment of mean IOP was 2.6 - 4.1 mm Hg among hypertensive versus 2.4 - 3.6 mm Hg among non-hypertensive in their 4 years follow up study. Beaver Dam study²² also showed an increment of SBP by 10 mmHg or more from baseline leads to 0.44 mmHg IOP rise and 0.59 mm Hg decrease in IOP in whom SBP decrease 10 mmHg or more from baseline, over 5 years of interval. Our study correlated with these studies, here we found that for every 10 mmHg rise in SBP, IOP was increased by 0.56 mmHg in RE and in LE 0.73 mm Hg. Wong TT et al.²³ and Michelle P.Y²⁴ also found a significant positive correlation between systolic blood pressure and IOP.

The Pearson correlation coefficient analysis for SBP and IOP of RE and LE was 0.29 and 0.34 respectively with probability value of $P < 0.0001$ in both eyes, which is statistically significant. Some cross sectional and longitudinal

studies had shown similar correlation between SBP and IOP like Baltimore eye study²⁵ and Beaver Dam Eye Study.²²

Ocular perfusion pressure (OPP), which regulates blood flow to the optic nerve depends on blood pressure and IOP.²⁶ Another cause of raised IOP secondary to raised SBP may be long standing SBP which might result in atherosclerosis also reflect a compromised pre-capillary arteriole that reduces ocular perfusion and disrupts auto-regulation mechanism of the vascular supply of optic nerve head.²⁰

The mean IOP was calculated for controlled and uncontrolled SBP patients and it came out to be 17.76 mm Hg in BE of controlled SBP and 20.19 mmHg and 20.64 mm Hg (RE and LE respectively) in uncontrolled SBP with z score being extremely significant. Samuel HM et al.¹⁵ also concluded that susceptibility of glaucoma was relatively high in patients with uncontrolled hypertension. This signifies patients with uncontrolled SBP have increased IOP.

In this study mean IOP increased with increasing range of SBP. Patients who had SBP between 100 - 120 mmHg had their mean IOP 17.50 mmHg in BE which increased to 21.29 mm Hg in BE with SBP more than 160 mm Hg, a 3.79 mm Hg linear IOP increase over the clinical spectrum of SBP levels was evident. Similar results were seen in Blue Mountain Eye Study,²⁷ Baltimore Eye Study,²⁵ study done by Minu Liz Abraham et al.²⁸ and Ravikiran Kisan et al.²⁹ (Figure 3).

This difference clearly indicates that with increasing SBP, IOP also increases simultaneously which if remained increased for longer period of time due to increased SBP will cause ill effects on optic nerve head and hence progress towards glaucoma. So, hypertensive patients need to keep their BP under control as well as glaucoma patients should be counselled to keep their BP under normal range failing which, it can add up to their disease progression.

CONCLUSIONS

Systolic blood pressure is significantly correlated with IOP and uncontrolled SBP was related to higher mean IOP. Also, higher the SBP higher was the IOP, and with every 10 mmHg increase in SBP, there was an average of 0.65 mmHg increase in IOP. IOP is one of the important modifiable risk factors for glaucoma which when not controlled in time can lead to permanent blindness. Therefore, patients who are known cases of hypertension and glaucoma, should be counselled to keep their BP under normal range failing which, it can add up to their disease progression.

Limitations

- The present study was a hospital based small sample size study which can't be generalised to the entire population. Therefore, large population-based studies are required.
- This was a cross-sectional study design, but these patients needed to be followed-up for further investigation and confirm the findings. So, there was a need for longitudinal studies.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

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