ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 06 | June - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUATION AND COMPARISON OF SYMPATHETIC AUTONOMIC FUNCTION BETWEEN HYPERTENSIVE AND NORMOTENSIVE SUBJECTS

Physiology

Radhika P Tutor, Department of Physiology, Vydehi Institute of Medical Science and Research Center, Bangalore

Roopasree B* Associate Professor, Department of Biochemistry, Little Flower Institute of Medical Science and Research, Angamaly*Corresponding Author

ABSTRACT

Hypertension is a prevalent life style disease that causes cardiovascular diseases associated mortality worldwide. Being a devastating endemic, hypertension require special emphasis to be studied for its complications and consequences. Existing literatures provide robust evidences of the disastrous effects of hypertension on autonomic function, but there are least evidences comparing it between hypertensive and normotensive adults. This study mainly concentrates on the effect of hypertension on sympathetic activity and its comparison between hypertensive and normotensive individuals. **Objectives:** To identify the differences of sympathetic autonomic function between hypertensive and normotensive individuals. **Methods:** A CASE and a CONTROL group each constituting with a sample of 44 subjects between the age group 25-65 years were recruited in the study. Autonomic function assessments were conducted with the help of Isometric Handgrip Test and Orthostatic Blood Pressure Test. Data were statistically analyzed using SPSS (Version 20.0). Descriptive statistics was presented as frequencies, percentages and mean± S.D. Statistical differences between the parameters of case and control groups were conducted by Mann- Whitney U-test and Paired T-test. $P<0.05$ was statistically significant. Results: Majority (54.5%) of the hypertensive patients belonged to the age group of 56-65 years. The mean difference in DBP after the Isometric Hand grip test in case group were not found to be higher than even 5 mmHg but, in the control group were greater than 15 mmHg with differences recorded among the groups being highly statistically significant (P=0.00). The mean SBP and DBP differences (after Orthostatic BP test) between lying down and sitting postures in both the cases and controls were found to be statistically significant with P values: 0.02, 0.02, 0.002 and 0.002 respectively. **Conclusions:** Hypertensive cases recruited for the study had impaired autonomic function when compared to the normotensive controls of the same age- group (25-65years).

KEYWORDS

Normotension, Autonomic Function and Orthostatic Hypotension

INTRODUCTION:

Hypertension is a very common and most prevalent public health challenge in both economically developing and developed countries of the world. Hypertension can be defined as a systolic BP level ≥140 mmHg and/or a diastolic BP level ≥ 90 mmHg. The number of hypertensive adults will reach 1.5 billion which is approximately 30% of the world population by the year 2025[1]. It is one of the inevitable risk factors of cardiovascular diseases related mortality. Poorly controlled Blood Pressure (BP) remains to be a strong reason of cardiovascular morbidity and mortality worldwide.

Globally hypertension is regarded as a major health problem, because of its magnitude and associated risks, the degree of its difficulty to be managed, high medical and social costs concerning the condition, and that it causes chronic cardiovascular and renal complications .The major risk factors for hypertension may include old age, familial history, overweight or obesity, decreased physical activity levels, use of tobacco and alcohol, marital status, occupation, education, socioeconomic status and BMI[2].

The autonomic nervous system has a decisive role in the control of blood pressure (BP) and heart rate (HR). The autonomic impairment in hypertensive patients and the succeeding vascular and cardiac changes may describe some of the correlation between hypertension and its associated risk factors for coronary artery diseases (CADs). [3] Therefore, Autonomic Nervous System can be a significant patho - physiological determinant in the development of hypertension. [4] Autonomic dysfunction originating in childhood may be considered as a precursor stage in those persons presenting with raised BP later in life.[5]

MATERIALS AND METHODS

SAMPLING

PARTICIPANTS:

- Normotensive and hypertensive individuals within the age group range 25-65.

SAMPLE SIZE:

CASE : 44 subjects already diagnosed with hypertension within the specified age group

CONTROL: 44 normotensive subjects within the specified age group.

SAMPLING TECHNIQUE: Stratified Random Sampling

The heterogeneous population was divided into 2 strata: Hypertensive and Normotensive. The samples were then recruited randomly from these strata considering the inclusion and exclusion criteria.

INCLUSION CRITERIA:

- Male and female patients between the age group 25 and 65 already diagnosed with hypertension.
- Male and female normotensive participants between the age group range 25-65.
- Willing participants.

EXCLUSION CRITERIA:

- Patients suffering from any major diseases like cancer, chronic infectious diseases etc.
- Patients undergoing any therapy or treatment.
- Hypotensive individuals
- Normotensive people suffering from any other serious medical conditions like renal tubular defects, hormonal excess or insufficiency etc. that can affect Blood Pressure.

STUDY DESIGN:

A descriptive and comparative Case- Control study between hypertensive and normotensive subjects.

STUDY SETTING: The study was conducted in patients and staffs of Little Flower Hospital, Angamaly, Ernakulam District, Kerala who visited the OP for weekly checkup.

ETHICAL CONSIDERATIONS

The study was approved by the Ethical Committee of Little Flower Institute of Medical Science and Research (LIMSAR), Angamaly, no: EC/08/2018 Permission was also obtained from the Medical Officer of the Primary Health Center to collect data from the patients.

STUDY DURATION:

A total of six months duration between December 2018 and June 2019 was taken for completing the study.

DATA COLLECTION:

A set of 2 groups; a CASE and a CONTROL each constituting with a sample of 44 subjects between the age group 25-65 years of age were recruited in the study. The case group of 44 hypertensive patients were randomly chosen from the Out Patient Department of LF Hospital Angamaly and the control group of 44 normotensive individuals were

chosen randomly from the staffs of various departments of the same hospital.

The subjects in the study were within the age group 25-65 and were recruited as 2 groups:

- Study group – Consisting 44 individuals with a previous history of hypertension or with an already diagnosed high BP.
- Control group – Consisting of 44 individuals within a normal blood pressure range. (Normotensive).

Data were collected from the patients only after getting written informed consent.

Assessment of autonomic (Sympathetic) function:

Isometric Handgrip Test: (IHT): Resting Diastolic Blood Pressure (DBP) of the subjects assessed pre- test using sphygmomanometer. The subjects are given a handgrip dynamometer and their maximum compression strength is noted from three consecutive readings taken. A rise in the DBP is recorded during isometric pressing of a handgrip dynamometer at an almost one third of the maximum contraction strength for 3–5 min. Blood pressure recordings are obtained at the other arm at 1 min duration. An increase in diastolic blood pressure is identified due to heart rate acceleration without any rise in peripheral resistance. The results are presented as the difference between the highest diastolic pressure during the test and the average diastolic pressure at rest. In normal healthy individuals it should be higher than 15 mmHg.[6,7]Special emphasis should be paid regarding the manner of performing the compression by the subject as many patients perform a Valsalva maneuver during this test and this can bias the test result.[8]

- **Orthostatic Blood Pressure Test (OBPT):** Hemodynamic reactions or responsiveness of the body to active standing were assessed in this test. Before the test, the subject was asked to rest in a supine position for about 4-5 minutes. The subject was then supposed to assume a sitting position abruptly and maintain it for about 1- 2 minutes. **Principle:** Directly after lifting to upright position, a substantial amount of blood gets redistributed to the lower extremities of the body (peripheral venous pooling), which substantially reduces the venous return and stroke volume of the heart. In order to maintain the necessary hemo-dynamic parameters, the organism initiates certain physiological compensatory mechanisms that can be divided into a rapid response with an abrupt fall in systolic and diastolic blood pressure and a visible acceleration of heart rate (first 30 s), a phase of early stabilization, which occurs approximately after 1–2 minutes, and a response to sustained orthostasis for more than 5 minutes.[9,7] A fall in systolic blood pressure by more than 20 mmHg and diastolic BP by more than 10 mmHg or the presence of certain symptoms like nausea, fatigue, dizziness etc. are considered to be abnormal [6, 7, 10].It is best performed to diagnose idiopathic orthostatic hypotension.[7]

STATISTICALANALYSIS:

Data were analyzed in the Statistical Package for Social Sciences (20.0). Descriptive statistics of the data were presented as frequencies, percentages and mean± SD. Comparison of means between the cases and controls were done using the Independent Sample T- test or Mann Whitney U- test and pre- and post- test comparison of means within the group were done using Paired sample T-test.

RESULTS

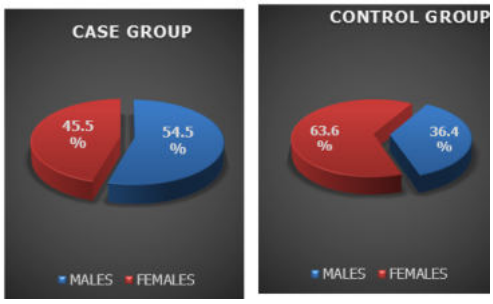
In the case- control observational study, a total of 88 subjects of which 44 cases with hypertension and 44 controls with normotension were incorporated for the analysis. Both descriptive statistics and comparison of means were conducted, and results were obtained.

SECTION 1: BASELINE CHARACTERISTICS OF THE DATA

Graph 1: Distribution of age among the study population

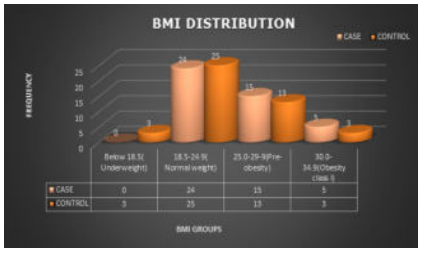
Graph 1 shows the age distribution of cases and controls in the study population. The mean age of the case group was distributed as 55.11±8.83 and that of control group were distributed as 39.11±11.81. Majority (54.5%) of the hypertensive patients belonged to the age group of 56-65 years and in that of control group majority (47.7%) of the normotensive individuals belongs to the age group of 25-35 years. Minor population (4.5%) of hypertensive cases belongs to the age group of 25-35 years and in that of control group minority (9.1%) of the normotensive individuals belong to the age group 46-55 years of age.

Graph 2 & 3: Gender distribution of the study population



Graph 2 shows that 54.5% of the case group were males and 45.5% were females. Graph 3 shows that in the control group majority (63.6%) were females and only 36.4% were males.

Graph 4: BMI distribution of the study population



Graph 4 shows the BMI distribution of the population and indicates that almost half of the cases (54.5%) and controls (56.8%) come under the category of normal weight. About 34.1% of the cases are pre-obese in nature and about 11.4% are obese in nature which attributes to the fact that obesity is a risk factor for hypertension. About 29.5% of the controls are pre-obese and 6.8% are obese and about 6.8% of them are underweight in nature.

Table 1: Distribution of Resting Systolic BP (SBP) in the Study population *ESC/ESH Hypertension Guidelines [11,12,13]

SBP RANGE (IN mmHg) *	CASE GROUP		SBP RANGE (IN mmHg) *	CONTROL GROUP	
MEAN±SD	129.09±21.43		MEAN±SD	113.41±11.19	
	F	%		F	%
OPTIMAL (<120)	12	27.3	OPTIMAL (<120)	26	59.1
NORMAL (120-129)	11	25.0	NORMAL (120-129)	9	20.5
HIGH NORMAL (130-139)	7	15.9	HIGH NORMAL (130-139)	9	20.5
GRADE 1-HYPERTENSION (140-159)	8	18.2	GRADE 1-HYPERTENSION (140-159)	0	0
GRADE-2 (160-179)	4	9.1	GRADE-2 (160-179)	0	0
GRADE-3(≥180)	2	4.5	GRADE-3(≥180)	0	0
TOTAL	44	100	TOTAL	44	100

Table 6 shows the distribution of resting systolic BP among the cases and controls. According to the ESC/ESH guidelines, among the case group about 27.3% had an optimal range of SBP, about 25% had normal range of SBP and about 15.9% had high normal SBP possibly attained through medication. Remaining 18.2%, 9.1% and 4.5% had

grade-1, 2 and 3 hypertensions respectively indicating the prevalence of systolic pre- hypertension and hypertension in most of the cases. Among the control group, 59.1% of the samples had an optimal resting systolic BP and the remaining 20.5% had normal and high normal SBP, with very few of the samples presenting with pre-systolic hypertension susceptive of anticipatory hypertension or due to any other reasons.

Table 2: Distribution of Resting Diastolic BP (DBP) in the study population

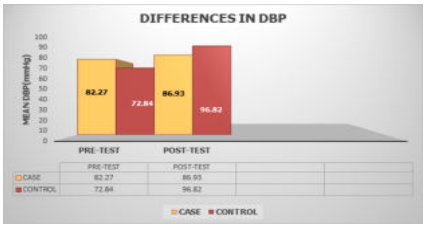
DBP RANGE (IN mmHg)	CASE GROUP		DBP RANGE (IN mmHg)	CONTROL GROUP	
MEAN±SD	82.27±11.78		MEAN±SD	73.07±7.64	
	F	%		F	%
OPTIMAL (<80)	15	34.1	OPTIMAL (<80)	27	61.4
NORMAL (80-84)	12	27.3	NORMAL (80-84)	15	34.1
GRADE 1(85-89)	11	25.0	GRADE 1(85-89)	2	4.5
GRADE 2(90-99)	5	11.4	GRADE 2(90-99)	0	011.4
GRADE 3(≥110)	1	2.3	GRADE 3(≥110)	0	0
Total	44	100.0	Total	44	100.0

*ESC/ESH Hypertension Guidelines [11,12,13]

Table 2 shows the distribution of resting DBP among the cases and controls. About 34.1% and 27.3% of the cases had an optimal and normal DBP respectively probably attained due to medication. About 25%, 11.4% and 2.3% had grade-1, grade -2 and grade- 3 diastolic hypertension respectively indicating the prevalence of both diastolic pre- hypertension and hypertension in the resting state. Among the controls majority 61.4% had optimal DBP, 34.1%had a normal DBP and only a few (4.5%) had grade – 1 diastolic hypertension possibly due to some other reasons.

SECTION 2: AUTONOMIC FUNCTION ASSESSMENT
2a: ISOMETRIC HANDGRIP TEST

Graph 5: Distribution of mean pre and post-test DBP among the cases and controls



Graph 5 shows the pre and post-handgrip test values of diastolic BP among hypertensive cases and normotensive controls. The mean pre-test values of the case group were distributed as 82.27mmHg and that of the control group were 72.84mmHg. The mean post-test values of the case group were distributed as 86.93mmHg and that of the controls were 96.82mmHg.

Table 3: Comparison of pre and post-handgrip test values among the study population.

GROUPS	N	MEAN DIFFERENCE IN DBP	STANDARD DEVIATION	Mann-Whitney U-VALUE	P VALUE
Hypertensive	44	4.66	7.502	-7.843	0.000
Normotensive	44	23.98	6.869		

Mann- Whitney U-test, P<0.05 are statistically significant

Table 3 shows the mean difference in pre and post- DBP values of isometric handgrip test among case and control groups. The mean difference in DBP after isometric handgrip test among the case group were distributed as 4.66±7.50 mmHg and that of the control group were distributed as 23.98±6.86 mmHg. A difference in DBP less than 15mmHg indicates impaired autonomic function. The mean difference in DBP after the test in hypertensive group were not found to be higher than even 5 mmHg but, the mean difference in the control group were obtained much greater than 15 mmHg. The differences recorded among the groups were also highly statistically significant (P=0.00) from which it can be inferred that hypertensive subjects had poor autonomic function.

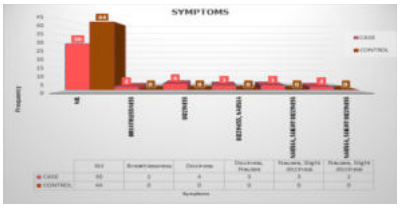
2. B: ORTHOSTATIC BLOOD PRESSURE TEST (OBPT)
2. B.1: General distribution of the data

Table: 4 Distribution of pre and post-OBP Test values among the study population

POSTURES	CASE			CONTROL		
LYING DOWN	SBP	MEAN	136.82	SBP	MEAN	134.32
		SD	18.01		SD	15.31
	DBP	MEAN	87.39	DBP	MEAN	75
		SD	11.83		SD	12.66
SITTING	SBP	MEAN	130.68	SBP	MEAN	113.86
		SD	18.97		SD	12.24
	DBP	MEAN	84.66	DBP	MEAN	78.64
		SD	12.26		SD	12.31
STANDING	SBP	MEAN	127.50	SBP	MEAN	113.86
		SD	19.42		SD	13.67
	DBP	MEAN	81.36	DBP	MEAN	79.77
		SD	13.39		SD	11.30

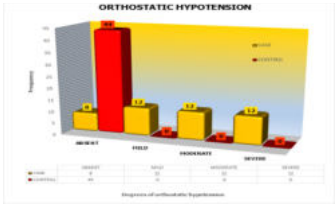
Table 4 shows the pre and post- Orthostatic BP test values of both cases and controls during lying down, sitting and standing postures. On recording the postural blood pressure changes of the cases, the mean SBP after lying down for 5 minutes were distributed as 136.82±18.01 mmHg, after sitting for 1-2 minutes were found to be 130.68±18.97 mmHg, after sudden standing for 1-2 minutes were distributed as 127.50±19.42 mmHg. Among the control group the mean SBP after lying down for 5 minutes were distributed as 134.32±15.31 mmHg, sudden sitting for 1-2 minutes showed a mean of about 113.86±12.24 mmHg, on standing the mean SBP were recorded as 113.86±13.67 mmHg. The mean diastolic BP among the case group after lying down for 5 minutes were distributed as 87.39±11.83mmHg, after sitting for 1-2 minutes were 84.66±12.26 mmHg and standing for 1-2 minutes had a mean of 81.36±13.39 mmHg. On examining the controls, the mean DBP after lying down for 5 minutes were found to be 75±12.66 mmHg, sitting for 1-2 minutes showed a mean of 78.64±12.31 mmHg, standing for 1-2 minutes had a mean of 79.77±11.30 mmHg. A sudden drop in systolic BP greater than 20mmHg or diastolic BP greater than 10 mmHg or presenting with certain symptoms are indicative of orthostatic hypotension and impaired autonomic function.

Graph 6: Distribution of symptoms of orthostatic hypotension among cases and controls



Graph 6 shows the distribution of symptoms of orthostatic hypotension among the study population. It is understood that the normotensive controls had not experienced any of the symptoms of orthostatic hypotension and majority (68.2%) of the hypertensive cases come under this category. Out of the remaining cases, 4.5% had breathlessness, another 4.5 % presented with nausea, 9.1% suffered from dizziness, 6.8% had nausea and slight dizziness and another 6.8% had both dizziness and nausea.

Graph 7: Distribution of orthostatic hypotension among cases and controls



Graph 7 shows the distribution of presence or absence or severity of orthostatic hypotension among the study population. Among the normotensive controls none of them showed BP variations and symptoms attributing to orthostatic hypotension and hence 100% of them were with no orthostatic hypotension. Among the hypertensive subjects, about 18.2% were free of symptoms and BP variations attributing to the condition and thus do not suffered from orthostatic hypotension. Among the remaining majority, each of a 27.3% had mild, moderate and severe orthostatic hypotension.

SECTION 2.b.2: Pair-wise comparison of OBPT values among cases and controls

Table 5: Pair- wise comparison of mean SBP Differences among the study population

GROUPS	N	POSTURE	MEAN DIFFERENCE IN SBP	SD	T-VALUE	P-VALUE
HYPERTENSIVE	44	Lying down-Sitting	6.136	13.506	3.014	0.004
	44	Sitting-standing	3.182	10.515	2.007	0.051
NORMOTENSIVE	44	Lying down-Sitting	.455	9.872	.305	.762
	44	Sitting-standing	.000	7.471	.000	1.000

Paired Sample T-Test, P<0.05 are statistically significant

Table 5 shows the comparison of mean differences in SBP after orthostatic BP test between hypertensive and normotensive subjects. A fall in SBP> 20mmHg is clinically significant. The mean difference in SBP from lying down to sitting in the cases were 6.136±13.506 mmHg and is statistically significant (P=0.004). The mean difference in SBP in cases while sitting to standing was 3.182 ±10.515mmHg, which is not statistically significant. Among the controls, the mean SBP difference from lying down to sitting was recorded as 0.455±9.872mmHg and that from sitting to standing was 0.000±7.471mmHg which aren't statistically significant. From the data it can be inferred that normotensive controls had good autonomic function as they had no much evidences of SBP variations and occurrence of symptoms.

Table 6: Pair- wise comparison of mean DBP Differences among the study population

GROUPS	N	POSTURE	MEAN DIFFERENCE IN DBP	SD	T-VALUE	P-VALUE
HYPERTENSIVE	44	Lying down-Sitting	2.727	9.551	1.894	.065
	44	Sitting-standing	3.295	8.137	2.686	.010
NORMOTENSIVE	44	Lying down-Sitting	-3.636	8.651	-2.788	.008
	44	Sitting-standing	-1.136	8.131	-.927	.359

Paired Sample T-Test, P<0.05 are statistically significant

Table 6 shows the comparison of mean DBP difference after OBPT between cases and controls. A fall in DBP> 10 mmHg is clinically significant. The mean DBP difference between lying down and sitting postures in cases were 2.727±9.551 mmHg and is not statistically significant. The DBP difference between sitting and standing postures were about 3.295±8.137 mmHg and is statistically significant (P=0.01). The mean DBP differences in controls after the test during the change of both postures were negative values (lying down – sitting: -3.636±8.651 mmHg, sitting- standing: -1.136±8.131 mmHg), indicating that there was a mean rise in DBP after the test in the control group. Hence the controls were free of orthostatic hypotension.

SECTION 2.b.3: Comparison of OBPT Values between case and control group

Table 7: Comparison of DBP and SBP differences between cases and controls

MEAN BP DIFFERENCE	N	POSTURE	MEAN DIFFERENCE	SD	T-VALUE	P-VALUE
Mean SBP Difference Between Lying Down and Sitting	44	CASE	6.14	13.506	-2.123	0.03
	44	CONTROL	.45	9.872		
Mean DBP Difference Between Lying Down and Sitting	44	CASE	2.73	9.551	-3.052	0.02
	44	CONTROL	-3.64	8.651		
Mean SBP Difference Between Sitting and Standing	44	CASE	3.18	10.515	-1.646	0.10
	44	CONTROL	.00	7.471		
Mean DBP Difference Between Sitting and Standing	44	CASE	3.30	8.137	-8.193	0.00
	44	CONTROL	1.14	8.131		

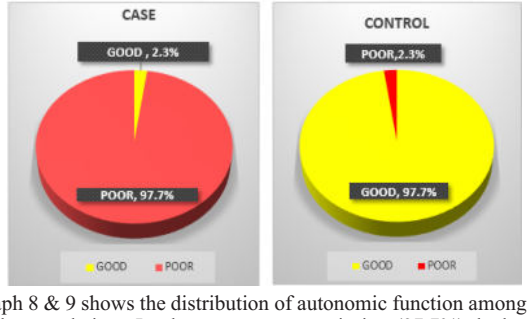
Mann- Whitney U-test, P<0.05 is statistically significant.

Table 7 shows the comparison of OBPT Between case and control groups. The mean SBP difference between lying down and sitting in the case group were 6.14± 13.50 mmHg and that of the control group were 0.45±9.87mmHg. The mean DBP differences after sitting for1- 2 minutes in the case group were distributed as 2.73±9.55 mmHg and that in the control group were distributed as -3.64±8.65 mmHg. Both differences between lying down and sitting in both the groups were found to be statistically significant with P values: 0.03 and 0.02 respectively. The mean SBP difference between sitting and standing in the case group were distributed as 3.18±10.51 mmHg and that of the control group were distributed as 0.00 ± 7.47 mmHg. The mean DBP difference in the case group were 3.30±8.13 mmHg and that of controls were 1.14±8.13 mmHg. The mean SBP difference between sitting posture and standing among the groups were not statistically significant but the DBP difference was found to be highly statistically significant with a P value of 0.00.

2. C: AUTONOMIC FUNCTION

2. C.1: Autonomic function among the study population

Graph 8 & 9: Distribution of autonomic function among cases and controls



Graph 8 & 9 shows the distribution of autonomic function among the study population. In the case group majority (97.7%) had poor autonomic function while in the control group majority (97.7%) had good autonomic function, indicating that hypertensive patients have autonomic dysfunction.

DISCUSSION

Hypertension is a life threatening public health challenge irrespective of age groups and is associated with several complications mainly affecting cardiovascular functions, sleeping patterns and quality, autonomic nervous system functions, level of stress, renal functions and much more. No comparative studies were conducted yet to analyze the possible differences of autonomic activity between hypertensive and normal subjects. The present study aims to

understand the effects of hypertension on autonomic function in hypertensive subjects and to compare those with normotensive subjects.

Existing literature reviews provide the cause and effect relationship of autonomic dysfunction in hypertension and there are least studies that depict the proof of autonomic impairment in hypertensive patients. This study analyzed the autonomic functioning of hypertensive group and compared it with the normotensive group coming under same age category. Also, presence of orthostatic hypotension among the cases and controls were assessed and an equal proportion (27.3%) of mild, moderate and severe conditions of orthostatic hypotension could be observed in the case group. Even though the grip strength of the majority cases were satisfactory there were very poor elevation in the Diastolic BP after completion of the test, which can be a major determinant of poor autonomic function in hypertensive individuals. Also increased stress levels in hypertensive patients can be due to increased release of stress hormones caused by elevated sympathetic discharge.[14,15]

LIMITATIONS AND SUGGESTIONS

The study was conducted in a small sample group and employing more number of samples in the future research may prove the facts and relationships in a better possible way. The study provides evidences only regarding sympathetic activity and the parasympathetic function is not assessed. Hence, it requires much more analysis for a detailed association.

CONCLUSION

Hypertension has evolved to be the most common routine health disorder worldwide and studies regarding its deleterious effects are gaining increased significance in the present scenario. Hypertension is known to cause several secondary health conditions affecting cardiovascular systems, sleep patterns, kidney functions, autonomic function etc.

Results of the handgrip test shows that hypertensive cases had impaired autonomic function as there were no significant post- test elevation in the diastolic BP. Data from graph 8 and 9 clearly states that, hypertensive cases showed a desired and clinically significant variation in either SBP or DBP or in both. Among the controls no clinically significant BP differences and occurrence of symptoms were present. Thus, it can be inferred that hypertensive cases had poor autonomic function whereas the normotensive controls had good autonomic function. Section 2.a describes the results of isometric handgrip test conducted among hypertensive cases and controls. Both tests conducted to assess the autonomic function among cases and controls separately and precisely shows that autonomic function is poor in patients with hypertension than in subjects with normotension.

Conflicts of interests: None
Financial Disclosures: None

REFERENCES

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J Global burden of hypertension: analysis of worldwide data.2005. Lancet 365: 217–223.
2. Shikha Singh,Ravi Prakash, Gyan Prakash Singh. "Prevalence and Associated Risk Factors of Hypertension: A Cross-Sectional Study in Urban Varanasi." International journal of hypertension .vol. 2017. https://doi.org/10.1155/2017/5491838
3. John Amerena, Stevo Julius, The Role of the Autonomic Nervous System In Hypertension, Hypertension Research, 1995, Volume 18, Issue 2, Pages 99-110, Released August 10, 2006, Online ISSN 1348-4214.
4. Knut Sevre ; et al. Autonomic Function in Hypertensive and Normotensive Subjects-The Importance of Gender 2001; June 1, 37:1351
5. Meghna P. Mansukhani, Naima Covassin, Virend K. Somers.Neurological Sleep Disorders and Blood Pressure, Hypertension AHAJournals ;3 Sep 2019;74:726–732.
6. Zygmunt, A., & Stanczyk, J. (2010). Methods of evaluation of autonomic nervous system function. Archives of medical science : AMS, 6(1), 11–18.
7. Van den Berg MP, Smit AJ. Bedside autonomic function testing in patients with vasovagal syncope. Pacing Clin Electrophysiol. 1997;20:2039–42.
8. Hilz ML, Dütsch M. Quantitative studies of autonomic function. Muscle Nerve. 2006;33:6–20.
9. Van Eck MM, Nicolson NA. Perceived stress and salivary cortisol in daily life. Ann. Behav. Med. 1994;16:221–227.
10. Jaradeh SS, Prieto TE. Evaluation of the autonomic nervous system. Phys Med Rehabil Clin N Am. 2003;14:287–305.
11. H.K Chopra, C.Venkata S.Ram. Recent guidelines for hypertension, A Clarion call for BP control in India. Circulation Research.28 March 2019:124:984-986
12. Williams B, Mancia G, Spiering W, et al.; ESC Scientific Document Group. 2018 ESC/ESH guidelines for the management of arterial hypertension.Eur Heart J. 2018; 39:3021–3104.
13. Whelton PK, Carey RM, Aronow WS, et al.. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines.J Am Coll Cardiol. 2018; 71:2199–2269.
14. Tanya M. Spruill, Chronic Psychosocial Stress and Hypertension, –Curr Hypertens Rep. 2010 Feb; 12(1): 1016.
15. Huang Y, et al.Poor sleep quality, stress status, and sympathetic nervous system activation in nondipping hypertension; Blood Press Monit. 2011 Jun; 16(3):117-123.