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Original research article

An endophenotype for hypertension "High sympathetic reactivity" association with high anxiety levels: Assessment of anxiety endophenotype in young medical students with parental history of hypertension-A cross sectional study

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Abstract

Introduction: Children of hypertensive parents exhibit endophenotype of high sympathetic reactivity & early parasympathetic attenuation. Studies on patients with panic disorder and high anxiety levels in past have shown to have sympatho-vagal imbalance with sympathetic over activity.

Materials and method: A cross sectional study was conducted with 120 sample size,60 in study group with parental history of hypertension and 60 without parental history of hypertension. Anxiety levels were assessed using HAM-A scale and compared between the two groups.

Results: Study group exhibited statistically significant sympathetic overactivity in the form of rise in diastolic blood pressure on isometric hand group exercise test. In these individuals anxiety levels were high compared to control group which was statistically insignificant.

Conclusion: The endophenotypes & illness co-segregate within families (prevalence of endophenotype is more in ill relatives of ill proband). Genetic predisposition to hypertension could be a potential risk factor for experiencing high anxiety levels. Findings suggest sympathetic over activity to be associated with high anxiety levels could be a future predictor of hypertension-an endophenotype. This finding needs longitudinal prospective study with large sample size to generalize the finding.

Keywords: Endophenotype, anxiety, sympatho-vagal imbalance, parasympathetic attenuation, sympathetic dominance, hamilton anxiety rating scale

Introduction

Endophenotype is a heritable biological trait which appears in both patient and their unaffected relatives and is state independent (Manifests in an individual whether the illness is active or inactive in them). The biomarkers (endophenotypes) are measurable in laboratory like neurocognitive performance deficit, electroencephalographic abnormalities dysfunctions. These endophenotypes & illness co-segregate within families i.e., prevalence of endophenotype is more in ill relatives of ill proband[1].

Offspring of hypertensive parents have endophenotype of high sympathetic activity and early parasympathetic attenuation exhibited as high anxiety levels, micro and macro circulation injuries with end organ damage as neuropathy, chronic renal failure & cardiovascular diseases in long run[2, 3, 4].

Anxiety is a basic human emotion, expressed towards an event that is perceived as a threat to self-esteem or ego and is characterized byfear and uncertainty. Anxiety of moderate level is good for individual's adaptation and productivity. Severe anxiety and arousal interfere with person's capacity to overcome difficulties by provoking fear, causing inhibitions & somatic changes (like tachycardia, palpitations, sweating, dry mouth, poor concentration) leading to maladaptation and poor academic performance.It is seen that any competition or mental task disorganizes our behavior and hamper motor performance. Studies on panic disorder and high anxiety have found sympatho-vagal imbalance in these individuals in the form of sympathetic over activity[5, 6].

Isometric hand group exercise test is a noninvasive physiological test used as a physical stressor to assess autonomic modulation. It is validated as a reliable test in unmasking pre-hypertension in normotensive children with parental history of hypertension. A raise in diastolic blood pressure in response to IHG test is considered as sympathetic over-activity (there is no cut-off limit for rise in DBP on IHG Test)[7, 8].

Hamilton Anxiety Rating Scale (HAM-A or HARS, 1959) is a clinician-based questionnaire. Maier *et al*. in their study concluded that HAM-A and its subscales are sufficiently reliable and validated scale to assess anxiety. It was designed with an intent to assess anxiety neurosis (not to assess pathological

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anxiety or problem)[9, 10].
Medical profession is a big stressor that drains the individual of his physical and mental health. If added risk factors like genetic susceptibility & unhealthy risk behaviors as sedentary lifestyle, eating junk foods, alcohol consumption & smoking exist together, it accelerates the underlying disease process. It is seen that Moderate arousal is good for decision making & better performance. Hence these young adults with ill probands endophenotypes, needs to be evaluated at the earliest to help them cope up with professional and personal life challenges gracefully[11, 12].

Objective of the study
Assessment of anxiety levels using HAM-A scale in young medical students with parental history of hypertension and comparing it with control group.

Materials and Methods
It is a cross sectional study, done between January 2017 to December2017in one of the medical college in north Karnataka, on first year MBBS students with age group was between 18-24years.Institutional Human ethical clearance and written informed consent of students was obtained prior to data collection. Using convenient sampling method, 200 students were screened for parental history of hypertension. Among them Sixty students reported about history of hypertension in either parent and included in study group. Another 60 students with no parental history of hypertension were selected from remaining students using systemic random sampling to form control group. Exclusion criteria was any history of drug intake for chronic illnesses, any h/o congenital heart diseases, K/C/O hypertension, neurological, endocrinal, psychiatric illnesses and habits like chronic Alcohol intake and Smoking were excluded from the study.
All standard procedures and instruments were used to collect Anthropometric & Physiological parameters. Krup's weighing scale (with near accuracy of ±0.5 Kg) and Stadiometer (to the nearest of 0.5cm**)** were used to measure weight and height respectively. Body Mass Index (BMI) was determinedusingQuetlet'sequation [Weight (kg)/Height (m^2)] as per Asian standard. Stethoscope & Standardized mercury sphygmomanometer (diamond deluxe BP apparatus, Pune India) were used to measure blood pressure[13, 14].
Handgrip Dynamometer-using Jammar hand grip dynamometer Inc. USA manufactured by INCO Ambala was used to measure sympathetic reactivity. The Hamilton Anxiety Scale, a subjective anxiety assessment scale was used to assess anxiety. It comprises of 14-questionsthat tests the severity of anxiety including both psychic and somatic symptoms. Its administration timeis around 10-15 minutes. Each 14 items arescored on a scale of0 (not present) to4 (severe)with a total score range of 0-56. The scoring <17 indicates-mild, 18-24 indicates-moderateand 25-30 indicates severe anxiety[9, 10, 13].

Statistical analysis
In present study descriptive and inferential statistical analysis has been carried out. Mean ± SD was used for continuous measurements & percentages for categorical measurement. Significance was assessed at 5% level. The study parameters significance between two groups was assessed using student's t-test and chi square test. For statistically significant P value of ≤0.05 was considered.

Results
The present study was conducted on 120 students, out of which fifty-six were males & sixty-four were females. The results of study are presented in the tables below:

Table1: Distribution of students on the basis of parental history of hypertension in single or both parents

Parental hypertension	Number	Percentage
Single parent hypertension	49	
Father	35	81.6%
Mother	14	
Both parents hypertensive	11	18.4%

Table 1 shows that 49 (81.67%) students had parental history ofhypertension in either of a parent. Out of 49 students 35 had a history of hypertension in father, 14 had a history of hypertension in mother & 11(18.33%) students had a history of hypertension in both the parents.

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Table 2: Comparison of demographic and anthropometric measurements between study and control group

Parameters	Case	Control	P value
Age (in years)	18.95±0.7	18.83±1.0	0.6
Height (in cm)	164.12±8.9	166.38±8.3	0.17
Weight (in KG)	64.6±13.3	63.1±13.1	0.55
BMI	24.08±3.8	22.83±4.1	0.09

Table 2 shows that the two groups did not differ much on demographic and anthropometric scale.Themean age of the study populationwas between 18-19 years, mean height was between 164-166 centimeters. Mean weight & BMI score was comparatively higher in study group but not statistically significant.

On baseline physiological parameters like PR (study group = 82.50±8.90: control group =79.07±8.45; p=0.032), SBP (study group=111.10±10.50: control group= 109.80±11.23; p=0.514), DBP **(**study group**=**74.65±5.86: control group=74.33±7.80; p= 0.802) were more among study group compared to control group which was not statistically significant.

The Study group showed rise in DBP (study group=98.90±11.26: Control group=89.52±9.88; P=0.0001*) during IHG-exercise which was statistically significant. Rise of SBP in study group compared tocontrol group during IHG test which was statistically significant (study group=142.73±17.40: Control group=129.37±12.73; P=0.0001*).

Table 3: Comparison of anxiety score on Hamilton anxiety scale (HAM-A) between study & control group

HAM-A	Study group		Control group		P value
	Frequency	Percent	Frequency	Percent	
< 17-Mild	52	86.7	54	90.0	
18-24-Moderate	6	10.0	3	5.0	0.744
25-30 -Severe	2	3.3	3	5.0	
Total	60	100.0	60	100.0	
Mean ± SD	11.15 ± 6.17		10.63 ± 6.73		0.662

Table 3 for comparing anxiety score on Hamilton anxiety scale (HAM- A) between study & control group showed that the anxiety scores were less in the control group, however this was statistically insignificant.

Table 4: Comparison between male and female gender on anxiety score on Hamilton anxiety scale (HAM-A) between the two groups

HAM A score	Study group	Control group	P value
	11.52±6.36	**10.88±6.87**	**0.601**
Gender			
Male	10.24±7.10	9.65±5.36	
Females	12.43±6.69	12.21±8.07	

Table 4 shows comparison of anxiety levels between male & females of the two groups, where in anxiety levels in study group was high compared to control group population but was statistically not significant.

Discussion

Our study found high sympathetic reactivity in study group in the form of rise in diastolic blood pressure to Isometric handgrip test compared to control group. In them anxiety levels were higher. On comparing male and female population on anxiety scores, study group female population scored high on anxiety levels but was statistically insignificant.

The association between anxiety & k/c/o hypertension is investigated in many cross sectional & prospective studies that have given inconsistent results. Some studies reported anxiety as a high-risk factor in causation of hypertension and also hypertensive patients having high anxiety levels. Some researchers do not support anxiety as a causative factor in acquiring hypertension and even have reported decreased BP in patients diagnosed of anxiety disorder[15, 16].

There is meager literature available that reports inheritance of anxiety in children with genetic susceptibility for hypertension. However sympathetic overactivity is associated with high arousal levels. The common emotional relationship & family environment they share also play an important role in disease progression.Studies in the past on assessment of anxiety levels in diagnosed cases of hypertension between 40-60 year's age group have found strong association of anxiety and hypertension. Anxiety causes short term increase in BP through renin angiotensin system, hypothalamo-pitutary-adernal axis dysfunction with sympathetic overactivation causing increased renal water-sodium retention that increasing the blood pressure. Further sympathetic overactivity causes abnormal hemodynamic changes, lipid metabolism & endothelial cell damage to increase the blood pressure[1, 17].White coat effect

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is best example of short-term increase in blood pressure due to anxiety state[16].
This sympathetic over activity in children of hypertensive parents can be termed as an endophenotype for hypertensive disorder, that has role in preventive research as it can recognize the individuals at high risk of developing disease in future.
Though our study has showed this phenomenon but few results were not statistically significant. Our study is first of its kind which has made an attempt to identify endophenotype. As it being a cross sectional study the limitation associated with it are applicable. We need long term cohort study to confirm this finding.

Conclusion

Findings suggest sympathetic over activity is associated with anxiety could be a future predictor of hypertension-an endophenotype. The endophenotypes & illness co-segregate within families i.e., prevalence of endophenotype is more in ill relatives of ill proband. Genetic predisposition to hypertension could be a potential risk factor for experiencing high anxiety levels. This finding needs longitudinal prospective study with large sample size to generalize the finding.

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