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A Case Control Study of the Genetic and Other Risk Factors of Essential Hypertension

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ABSTRACT

Introduction-Essential hypertension, an important cause of worldwide mortality and morbidity, has modifiable and nonmodifiable risk factors. We tried to find a causal relationship between development of essential hypertension and various risk factors especially genetic factors.

Methods-In this case control study, 110 essential hypertension patients and 50 age and sex matched normal healthy individuals were selected. Detailed physical examination was done and history was taken including pedigree analysis. Serum total cholesterol, triglyceride, HDL-C and LDL-C were estimated.

Result-Most of the cases were of the age group 50-59 years, with a mean age of 57.1 years. Of the female cases, the age group 60-69 years was mostly affected. Diabetes mellitus, coronary artery disease, hypothyroidism, cerebrovascular accidents and obesity were associated more with cases in comparison to controls. Out of 110 cases, 66 cases (60%) had family history of hypertension; either father (24.5%) or mother (35.4%) was hypertensive. Both parents were hypertensive in 27 cases (24%). This familial trend was seen in brothers and sisters as well as in offsprings.

Conclusion-Several factors are associated with essential hypertension. Modification of some of those factors may beneficially affect the long term effects and complications of hypertension. Early detection of many factors and suitable measures may be important in the prognosis and course of hypertension related outcomes. Further research with a larger and diverse population is required to confirm these findings.

Keywords- Essential hypertension, risk factors, hereditary basis

INTRODUCTION

Essential hypertension is common in developing countries, and rates of awareness, treatment, and control are low. [1] The prevalence of hypertension, with its complications, is increasing. [2] Complications of hypertension such as cardiovascular and cerebrovascular death, are a major cause of mortality worldwide. Several hypertension risk factors seem to be more common in developing countries than in developed regions. [1]

Essential hypertension has modifiable and nonmodifiable risk factors. Modifiable risk factors include obesity, dyslipidemias, smoking, physical activity, stress, salt intake, etc. Nonmodifiable risk factors are age, sex and genetic factors among others. Genetic, environmental and demographic factors and their interaction determine an individual's risk for hypertension. [3] The quantitative contribution of genetic factors to blood pressure variance is estimated to be about 30%, however, the genetic background of essential hypertension is complex and currently not fully understood. [4] However, despite the considerable research effort, it is still difficult to identify all genes and/or other genetic determinants leading to essential hypertension and other cardiovascular diseases. [5] Family studies demonstrated the contribution of genetic factors to the development of primary hypertension. [6] With this background we sought to find a causal relationship between development of essential hypertension and

various risk factors especially genetic factors (hereditary inheritance).

MATERIALS AND METHODS

In this case control study 110 essential hypertension patients were recruited as cases from the outpatient department of a tertiary care medical college and hospital. 50 age and sex matched normal healthy individuals who did not have any disease were selected as controls. Duration of the present study was 1 year and 8 months. All patients who were eligible for participation in the study were appropriately screened and enrolled after obtaining informed consent. Detailed physical examination and history was taken from all subjects. Pedigree analysis of all participants was done. Exclusion criteria included participants who were smokers, suffering from acute or chronic diseases like diabetes mellitus, coronary artery disease, stroke, thyroid disorders etc, hepatic or renal impairment, unusual dietary habits.

Blood was collected from all subjects after overnight fasting and estimation of serum parameters done.

Serum total cholesterol and triglyceride were estimated by enzymatic methods. [7,8] Serum HDL-C was assayed by the method of Warnick et al. [9] Low-density lipoprotein cholesterol (LDL-C) concentration was then calculated from the concentration of TC, HDL-C and TG using the method of Friedewald and Levy. [10]

To avoid the possible dispersion of results, all the samples were processed at the same time, at the end of the recruitment process.

Statistical analysis of data was performed using SPSS software, and inferences were drawn. p values of <0.05 and <0.001were considered to be statistically significant and highly significant respectively.

RESULTS

Table 1. Age and sex distribution of cases and controls

Age in years	30-39		40-49		50-59		60-69		70-79		Mean (of age, in years)
Sex	M	F	M	F	M	F	M	F	M	F	
Cases	7	0	17	0	39	6	20	10	7	4	57.1
Controls	3	0	7	0	17	3	9	6	4	1	58.8

Table 2. Prevalence of risk factors in cases and controls

Risk factors	DM		CAD		Hypothyroid		CVA		Obesity	
	No.	%	No.	%	No.	%	No.	%	No.	%
Cases	26	23.6	22	20	4	3	35	31.8	87	79
Controls	8	16	3	6	1	2	3	6	13	26

Table 3. Serum lipids (Mean ± SD, in mg/dl) in cases and controls

	Total cholesterol	LDL-C	HDL-C	Triglyceride
Cases	195.4±23.48	115.43±15.61	33.69±7.28	231.45±84.06
Controls	182.6±10.58	106.76±13.84	45.34±12.42	150.34±34.10

For serum cholesterol-

t test results

P value and statistical significance:

The two-tailed P value equals 0.0003

By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval:

The mean of Group One minus Group Two equals 12.8000

95% confidence interval of this difference: From 5.9370 to 19.6630

SEM : for cases-2.2387, for controls-1.4962

Intermediate values used in calculations:

t = 3.6837

df = 158

standard error of difference = 3.475

For serum LDL-C-

t test results

P value and statistical significance:

The two-tailed P value equals 0.0009

By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval:

The mean of Group One minus Group Two equals

8.6700
95% confidence interval of this difference: From 3.5888 to 13.7512
SEM: for cases-1.4884, for controls-1.9573

Intermediate values used in calculations:
t = 3.3701
df = 158
standard error of difference = 2.573

For serum HDL-C

t test results

P value and statistical significance:
The two-tailed P value is less than 0.0001
By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval:
The mean of Group One minus Group Two equals -11.6500
95% confidence interval of this difference: From -14.7449 to -8.5551
SEM : for cases-0.6941, for controls-1.7565

Intermediate values used in calculations:
t = 7.4349
df = 158
standard error of difference = 1.567

For serum triglyceride-

t test results

P value and statistical significance:
The two-tailed P value is less than 0.0001
By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval:
The mean of Group One minus Group Two equals 81.1100
95% confidence interval of this difference: From 56.7354 to 105.4846
SEM: for cases-8.0148,for controls-4.8225

Intermediate values used in calculations:
t = 6.5724
df = 158
standard error of difference = 12.341

Table 4. Detailed breakup of levels of serum lipids (in mg/dl) in cases and controls

	Total cholesterol			LDL-C			HDL-C			Triglyceride			
	160-179	180-199	>200	<130	130-159	>160	<35	35-65	>65	<200	200-400	400-1000	>1000
Cases	25	49	34	93	17	0	54	56	0	36	65	9	0
Controls	22	27	1	45	5	0	2	36	12	39	11	0	0

Table 5.Pedigree analysis: number of relatives having hypertension

	Father	Mother	Brother	Sister	Son	Daughter	Distant relatives
Cases	27	39	41	44	20	8	10
Controls	4	6	5	4	1	1	2

DISCUSSION

In the present study, most of the patients were of the age group 50-59 years, with a mean age of 57.1 years (table 1). This result is consistent with previous studies, where it had been reported that because of its high prevalence and sustained impact as age increases, hypertension emerged as the dominant risk factor for cardiovascular disease in older persons. [11] Regarding sex distribution of development of hypertension, it was noted that of the female patients, the age group 60-69 years was mostly affected (table 1). The mean age and sex distribution of controls were kept near the mean age of cases to eliminate any age induced bias in other risk factors. Stiffer large arteries likely contribute to the greater prevalence of systolic hypertension in elderly women and may partly explain the acceleration in postmenopausal cerebrovascular and cardiac complications. [12]

The dependence of blood pressure on a balance between superoxide and nitric oxide may be amplified in diabetes. It has been shown that the first occurrence of sustained hyperglycemia in type I diabetes causes hypertension. [13] Diabetic nephropathy is the commonest cause of hypertension in patients with type 1 diabetes. Patients with type 2 diabetes can develop renal disease, but hypertension commonly occurs without abnormal renal function. Insulin resistance and diabetes can

precipitate hypertension by stimulating the sympathetic nervous system and the renin–angiotensin system, and promoting sodium retention. Patients with diabetes also have increased vascular reactivity. [14] In the present study also 23.6% cases had diabetes mellitus (table 2).

The association between obesity and hypertension is well recognized. [15] Hypertension is often associated with central obesity. [14] Our study noted 79% cases with obesity whereas only 26% controls had obesity (table 2). Again, hypertension has been well linked to coronary artery disease [16] and in our study 20% cases had coronary artery disease (table 2). Hypothyroidism can cause hypertension, as recognized by workers. [17,18]

Hypertension treatment guidelines include recommendations focused on the reduction of hypertension-related conditions like stroke. Thus, associations between stroke and hypertension are very well documented. [19]

In our study (tables 3 and 4) dyslipidemias were associated with hypertension. The increase in total cholesterol levels were highly significant in cases compared to controls, a finding supported by other workers, who found that on lowering of serum cholesterol, hypertension was decreased. [20] Also, extremely significantly increased triglyceride levels were seen in cases, with respect to controls, a fact found by other researchers, who stated that triglycerides and triglycerides to high-density lipoprotein cholesterol ratio are strong predictors of incident hypertension. [21] Low HDL-C and high LDL-C are established associations of hypertension. [22,23] In the present study also, serum LDL-C and HDL-C levels were extremely significantly increased and decreased respectively, in cases when compared to controls.

In our present study, special emphasis was given on familial inheritance of hypertension. For the above purpose, detailed pedigree analysis was done. From the analysis, it was seen that familial trends definitely play an important role in genesis of hypertension. Out of 110 cases, 66 cases (60%) had family history of hypertension; either father (24.5%) or mother (35.4%) was hypertensive. Both parents were hypertensive in 27 cases (24%) as shown in table 5. This familial trend was seen in brothers and sisters as well as in offsprings. Family history of hypertension is a well established association. [24] Hypertension in both mothers and fathers has a strong independent association with elevated BP levels and incident hypertension over the course of adult life. [25] An increase in the number of family members with hypertension was associated with an increasing prevalence of hypertension and blood pressure in the probands, independent of conventional risk factors for hypertension. Family members of hypertensive subjects may need to be treated in primary prevention efforts related to hypertension. [26] Elevated blood pressure emerges well before adolescence among children with a family history of hypertension and the family environment appears to play an important role in its development. [27]

This study has limitations that must be considered. To assess serum parameters, various methods were used. These parameters can be estimated by other methods, but the present methods were employed as those were the most commonly used, time tested and standard methods. Also, number of patients in the study groups was not large. Thus, care must be taken in extrapolating the present findings to other populations.

Despite these limitations, we believe our study points out that many of the above mentioned risk factors can be changed by primary prevention. In the long run, these can affect the morbidity and mortality of an individual. Nevertheless, our work can only be validated if more research is done for a longer period in a larger number of patients with a more diverse population.

CONCLUSION

Several factors are associated with essential hypertension. Modification of some of those factors can affect the long term effects and complications of hypertension. Early detection of many factors and suitable measures are important in the prognosis and course of hypertension related outcomes. Still, further research with a larger and diverse population is required to confirm these findings.

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