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Development and Validation of a Predictor Equation to Detect Hypertensive Risk Population

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Abstract

Background: *Primary prevention model has been the major arena of treatment modality in the modern medicine. Strategizing towards this, a predictor equation to identify the risk population of hypertensives was computed in this study.*

Method: *Our study included 80 hypertensives and 40 normal subjects and it was a case control study. This study was done among both genders selected from Indian population. Strict inclusion and exclusion criterion were framed.Parameters such as height, weight, body mass index, systolic blood pressure, diastolic blood pressure and total leucocyte count were estimated. The controls were age and sex matched and selected from the normal population.*

Result: *Statistical Discriminant analysis was done using our data to derive an equation to identify the risk population of hypertension. The stepwise discriminant analysis identified four variables: Diastolic blood pressure, Total count, Weight and Age as significant contributing factors for hypertension. The discriminant function correctly assigned 79 out of 80 Cases (98.8% accuracy), and 38 out of 40 Controls (95% accuracy), the overall accuracy of prediction in assigning a person as a hypertensive or normal was 97.5%.*

Conclusion: *Applying translational significance to research is of utmost important and the ease-of-use prediction formula is the need of the hour. This formula enhances identification of risk population of hypertensives in a simple clinic set up and its importance is ameliorated with the total count used in the formula, emphasizing the patho-inflammatory state in early stages of hypertension.*

INTRODUCTION

Hypertension is considered as an entrenched global disease and a flagrant growing problem of non-communicable diseases. Several studies have identified that the overall prevalence of hypertension in India is found to be around30%, predominantly among the urban population, to about 33.8% (1) . Studies have projected that the incidence of hypertension could go up to 22.9% for Indian men and 23.6% for Indian women by 2025 (2). This increase in the trend of hypertension among the urban population are due to the modernization of today's world. There are several known hypertensive risk factors such as obesity, dietary habits, smoking, alcohol, sedentary lifestyle and other stressors of modern life contributing to the adverse outcome of hypertension. A study by Wang et al has proposed that the risk of developing hypertension is higher among those with pre hypertension, also the incidence is higher among those above 60 years of age than below 50 years and there was no sex difference in the development of hypertension (3). Studies have proposed that among the younger population, the increase in upper and lower body fat distribution increases with age and there is increased risk of hypertension and hypertensive heart disease (4). The complications of hypertension range in affecting several systems of the body predominantly the vascular, cardiac, and renal. Ventricular hypertrophy, heart failure, atherosclerosis, stroke, retinopathy are few of the complications seen commonly in practice (5). The patients may present

to the physician with these complications directly, as hypertension is also considered a silent disease and may remain unnoticed. The early detection of hypertension with essential parameters would be the initiative in curbing the disease. The diagnosis of hypertension begins in the clinical setup with the traditional auscultatory method of recording. There are limited evidences to identify risk population of hypertensives using simple mathematical techniques (6) and up to our knowledge no equation is being derived for the Indian Population. The objective of our study was to ascertain a simple equation to predict hypertensives with basic outpatient parameters.

METHODOLOGY

Design and Setting**:** This was a Case Control study and the data was collected directly from the participants.

Ethics Approval and Consent to participate: The study was approved by the ethics committee of Institution with approval CHRI/PG/2016/5. This study was performed with proper clinical practice and with suitable regulatory requirements in fulfilment with all ethical principles.

Participants and Recruitment: The participants for the study were selected from the medicine unit in Tertiary hospital of age between 20-60 years of either sex. After obtaining written informed consent form, 80 Hypertensive subjects and 40 controls (normal population) were included in this study.

Inclusion and exclusion criteria:

Our study included participant of either sex with history of hypertension and on medical treatment, wherein Hypertension is defined as systolic blood pressure>=140mmHg, and diastolic blood pressure >=90mmHg (ESC 2018 guidelines).

Subjects with history of other chronic medical disorders, pregnant women, women during their mensuration phase, subjects with history of infection in past 3 months, obese individuals, regular alcoholics and smokers were not included in this study.

Controls: The control participants were selected from normal population of age and sex matched, with no history of any illness and not any medications.

Data Collection: The subject's biographic data were collected. The participant's height and weight were measured. Blood pressure measurement was done using standardised technique using American heart association guidelines. 5 ml of blood sample was collected for total leucocyte count estimation, which was analysed in an automated analyser, Beckman Coulter LH 780. The reports were collected and the parameters were entered in excel sheet and computed.

- ✓ Height, weight, BMI
- ✓ 3 recordings of Systolic and Diastolic pressure and their average taken
- ✓ Total Leukocyte count
- ✓ Statistical Analysis was done using the SPSS software version 21.

RESULTS

Discriminant analysis was done to formulate the mathematical model to predict the hypertensive risk group using the coefficients: age, weight, diastolic blood pressure and total count (Tables 1,2, and 3).

DISCUSSION

A discriminant analysis was done using our data to derive an equation to identify the risk population of hypertension. The stepwise discriminant analysis identified four variables, Diastolic blood pressure, Total count, Weight and Age as significant contributing factors for hypertension. The canonical discriminant function coefficients for the variables are given in the table 1.

Based on this, a Predictor equation was derived,

Z = (subject age x 0.03559) + (subject weight x 0.04563) + (subject diastolic BP x 0.11592) + (subject total count x 0.00042) - 17.68178 Equation (A)

To identify a person being in Cases (Hypertension patients) or in the control group - age, weight, diastolic pressure value, and Total count are to be substituted in equation (A). If the value of Z is 0.0005 or more (i.e., average of [1.200 + (-2.399)]/2) then the subject can be assigned to the Cases group, and if Z is less than 0.0005, the individual is considered as in the control group.

The prediction accuracy of the discriminant function has been tested by assigning values in the equation (A) with the data used for constructing the equation and classifying as Cases or Control. The results of

classification are given in Table 3. The discriminant function correctly assigned 79 out of 80 Cases (98.8% accuracy), and 38 out of 40 Controls (95% accuracy), as shown in table 3.

The overall accuracy of prediction using the function in assigning a person as a hypertensive or normal was 97.5%.

Predictors of hypertension:

Age: There are several studies highlighting the association of the above parameters used in the predictor equation and their influence in hypertension. Several studies among different populations have correlated the age-related changes and risk of developing hypertension. A study by Gurven et al, underwent a longitudinal study among the Tsimane farmers relating the age related increase in the development of hypertension, they have suggested that prevalence of hypertension for men and women were 3.9% and 5.2% respectively, they also suggested that there was an increase of 2.86 and 0.95mmHg of systolic and diastolic pressures among women and 0.91 and 0.93mmHg increase in systolic and diastolic pressures for men along with the increase in age (7) . Hence age could play a role in development of hypertension and could be an important predicting component in risk stratification.

Weight: There has been a positive relation between the obesity and hypertension. One of the pathophysiological mechanisms in hypertension is the alteration of the pressure natriuresis. Studies have pointed out the derangement of this pressure natriuresis by obesity leading to sustained hypertension. Richard et al have commented on this mechanism, they have suggested that alteration in several mechanisms such as increased sympathetic tone, hyperinsulinemia, enhanced activity of rennin angiotensin system, structural changes in the kidney and excess of adipokines, such as leptin, which are produced by the fatty tissues could alter the pressure natriuresis contributing to obesity related hypertension (8). A study by Heianza et al, among the Japanese population, on comparing the body mass index with the development of hypertension, have proposed that those subjects with elevated body mass index at the initial stages and those with lifetime high body mass index were prone to the development of hypertension than compared to those with normal index (9). Our discriminant analysis included the weight of an individual as one of the parameters in identifying the risk population of hypertension.

Total Count: Total white blood cell count is considered as easily available, highly standardized and a very economical inflammatory marker that is routinely used (10). Studies have shown a relationship between the high normal total leucocyte count and its component as an inflammatory response in several metabolic syndromes and its proportional increase with increase in number of metabolic syndrome(11). Our study highlights this additional pathogenic feature of leucocytes as a marker of vascular inflammatory response in addition to being an evident marker of infection and tissue damage. Any chronic low grade inflammation leading to raised WBC's may be due to surge in sympathetic nervous system response, in turn leading to increased catecholamine levels and a more rise in blood pressure, eventually leading to sustained hypertension.

The role of total white blood cell count among hypertensives has been substantiated with various studies; it was shown that there is significant elevation of the total white blood cell count among the hypertensives and more predominately among the pre hypertensives and within 1 year of diagnosed hypertension (12). It could be hypothesised from several studies that an inflammatory process underlying hypertension could have started at an earlier time before the clinical evidence of hypertension. Hence, the total count in the discriminant equation could be of benefit in identifying the risk population of hypertensives and also tell us the patho-inflammatory status in hypertension.

Diastolic blood pressure: The diastolic pressure has been used here as one of the predictor factors of hypertension. There are some supporting evidences that diastolic pressure has independent association to the complications of hypertension. A prospective collaborative study in University of Oxford UK, have studied relation of diastolic pressure and its risk for stroke and the age factor. They have noted that with a difference in diastolic pressure of more than 27 mmHg, there was fivefold difference in stroke risk and it was more evident in middle age groups than the old age (13). Another study by Nancy cook et al have studied the effect of reduction of diastolic blood pressure by 2mmHg in the mean population distribution as a measure of primary prevention could cause a relative decrease in the rate of stroke and coronary heart disease incidences (14). A part of our study showed a linear rise in total leukocyte count and neutrophil lymphocyte ratio along with rise in diastolic pressure (15) .

To our knowledge this is a first kind of study in formulating a predictor equation to identify hypertensive risk group in the Indian population. Though this background might be a supporting evidence, further

analysis needs to be done on the predictor equation on varied subsets of population, gender, races and community to ascertain its validity in the predicting hypertensive risk group.

Few limitations of our study are: Reduced sample size, sample is limited to the Indian subset of population, the parameters and blood pressure are based on a single measurement.

CONCLUSION

This risk scoring prediction equation comprising age, weight, diastolic blood pressure and total count could stratify population at risk of developing hypertension.

The Predictor equation to identify the risk population of Hypertensives(Z):

Z = (subject age x 0.03559) + (subject weight x 0.04563) + (subject diastolic BP x 0.11592) + (subject total count x 0.00042) - 17.68178.

The major highlight of the equation is the use of total count, which could signify the underlying inflammatory process that begins even at stage of prehypertension. This risk calculator could serve as an early diagnostic tool in detecting hypertension. Also, this predictor equation can be applied to individuals with prehypertension, to estimate the risk of developing hypertension in a simple clinical setup or at a peripheral health centre. To further validate the veracity of this function, samples from different hospital sources and communities will have to be collected and equated. This might enhance the prediction accuracy of this discriminant function.

Impact:

Risk prediction model has been identified for hypertension under varied subset of population. This study contributes the data prediction from Indian subset of population and a derivative equation that can be used to predict hypertensive group of population. Early detection of hypertensive population is of utmost importance in strategizing the treatment protocol and preventing complications. This cost-effective primary prevention equation model can curb the risk of hypertensive complications.

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Disclosure Statement: The author(s) report no conflict of interest, None declared.

Ethics Approval and Consent to participate: The study was approved by the ethics committee of Chettinad Hospital and Research Institute. The study was performed with fulfilment of the ethical principles mentioned in declaration of Helsinki, which are with proper clinical practice and with suitable regulatory requirements.

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Table 1: Canonical Discriminant Function Coefficients - Unstandarized

	Function
	1
Age	0.03559
Weight	0.04563
Diastolic Blood Pressure	0.11592
Total Count	0.00042
(Constant)	-17.68178
Unstandardized coefficients	

Table 2: Functions at Group Centroids

Functions at Group Centroids	
	Function
Group	1
Cases	1.200
Control	-2.399
Unstandardized canonical discriminant functions evaluated at group means	

Table 3: Accuracy of prediction comparing cases and controlOriginal Group vs. Predicted Group

		Predicted Group		
Original Group	Statistics	Cases	Control	Total
Cases	Count	79	1	80
	Row %	98.8	1.3	100.0
Control	Count	2	38	40
	Row %	5.0	95.0	100.0
Total	Count	81	39	120
	Row %	67.5	32.5	100.0
Accuracy of Prediction: 97.5%				