ORIGINAL ARTICLE

Correlation Of Hematocrit And Hemoglobin With Obesity, Serum Lipids And Aldosterone In Newly Diagnosed Hypertensive Patients

Sadiqa Syed, Shazia Shakoor, Masood A Qureshi

Abstract

Objective: To determine the relationship of obesity indicators with certain hemodynamic and metabolic cardiovascular risk factors, at the initial diagnosis of hypertension in a random population, in search of a treatable cause

Methods: A case control study was conducted on 201 subjects aged between 25-60 years, diagnosed primarily as prehypertensive or hypertensive stage I and II , selected from five general practitioners clinics in Karachi. Estimated of hematocrit, hemoglobin, triglycerides, low density lipoproteins, serum potassium level and aldosterone was done. Their body mass index and waist hip ratio were calculated by measuring body weight, height, waist and hip circumference. The values obtained were compared with 75 controls with normal blood pressure.

The mean and standard deviation were computed. Analysis was done by SPSS version 15.LSD test was applied to compare pair-wise group. Pearson's correlation was applied to find out association of different variables with one another, within each of the four groups

Results: The overall percentages of overweight and obese subjects were higher in all four groups. The mean hematocrit and hemoglobin levels were highest in HTN stage –I (44.7±5.25 and15.4±2.20 respectively). Hemoglobin was strongly correlated to systolic blood pressure and waist hip ratio in both hypertension stages-I and II ($p<0.01$). Whereas hematocrit was positively correlated to body mass index, triglycerides, serum potassium and aldosterone levels in both stages of hypertension ($p<0.01$)

Conclusion: High hematocrit, hemoglobin, triglyceride levels, visceral fat accumulation and aldosterone secretion are important and independent risk factors for hypertension.

Key words: hypertension, hematocrit, hemoglobin, triglyceride, aldosterone

Introduction

Hematocrit (Hct) or packed cell volume represents the cellular portion of blood mainly red blood cells, expressed as percentage (% vol/vol) and is the major determinant of whole blood viscosity (WBV). [1] Other factors that contribute to blood viscosity in addition to Hct include plasma proteins, plasma lipids and other rheological factors. [2] It has long been known after Poiseuille-Hagen equation, that a strong association exists between WBV and hypertension (HTN), as hyperviscosity affects peripheral resistance (PR), and thus blood pressure (BP), not only by increasing resistance to flow and workload on heart, but also by hindering vasodilation. [3]

Hct above the normal range along with related hematological variables such as hemoglobin (Hb), red blood cell count and mean corpuscular volume, predispose to both arterial and venous thrombosis, in primary and secondary erythropoiesis [4] and may be a responsible factor in causing cerebral ischemia, especially if associated with inflammation.[5] Hb the oxygen carrying pigment in the blood, is an important nitric oxide (NO) buffer and a modulator of its bioavailability and hence plays a central role in vascular function.

✉ **Sadiqa Syed**
Professor of Physiology,
College of Medicine, Princess Norah University, Riyadh
Email: sadiqasyed@yahoo.com
Shazia Shakoor
Assst. Professor, Physiology
Bahria University Medical and Dental College, Krarchi
Masood A Qureshi
Director Post Graduate Program, DUHS, Krarchi
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Population-based studies have consistently demonstrated that on average Hb is raised in patients with essential HTN; thus it is suggested that Hb-dependent mechanism contributes to endothelial dysfunction in HTN by influencing availability of NO. [6] Hb, by a series of biochemical processes including NO oxidation and nitrosylation of iron molecules and sulfur containing amino acids in globin molecules, neutralizes the NO very effectively. This direct negative effect on NO availability might explain the link between high Hct and cardiovascular disease (CVD).[7] A study revealed that Hb level > 17 g/dL is associated with coronary artery disease (CAD). [8]

Several epidemiological studies supported the evidence that elevated blood viscosity and Hb concentration are related to HTN, insulin resistance (IR) [9], metabolic syndrome, severe obesity and peripheral atherosclerosis in adults [10]. A study showed that low density lipoprotein cholesterol (LDL) is the principal lipid that independently influences the WBV [11], whereas other studies suggested that high triglyceride (TG) and low HDL levels are responsible for elevating WBV and promoting atherosclerosis. [12, 13] WBV is inversely related to flow and may predispose to IR and type 2 diabetes mellitus, by limiting delivery of glucose, insulin and oxygen to metabolically active tissues [14]

Prospective studies have revealed that intraperitoneal and posterior subcutaneous fat mass is strongly linked with dyslipidemia and IR [15]. Moreover free fatty acids released from visceral adipose tissues have been shown to increase IR and aldosterone production.[16] Plasma renin and aldosterone levels both, have been reported to be three folds greater with secondary erythrocytosis compared to controls. [17]

Epidemiologists and biologists have been trying to identify new risk factors, particularly modifiable risk factors that could explain some of the variability in HTN

and CVD, not explained by traditional risk factors. Thus over hundred risk factors have been proposed by Framingham Heart Study. This study focuses on finding an association and correlation between hemodynamic factors Hct and Hb, plasma lipids concentration (TG, LDL), body fat composition, reflected by Body mass index (BMI), Waist hip ratio (WHR) and aldosterone hormone.

Subjects and Methods

It was a case control study with purposive sampling, carried out on 276 subjects, aged between 25-60 years, selected from five general practitioners clinics in Karachi and were categorized into four groups according to 7th JNC report. [18] The control group (A) had normal systolic (SBP) and Diastolic BP (DBP). The prehypertension (pre-HTN) group (B) had systolic BP between 120-140 mmHg and diastolic BP >80 and < 90 mmHg, hypertension stage-I (C) with SBP >140 and <160 mmHg; DBP >90 and <100 mmHg and Stage-II (D) with SBP >160 and DBP >100 mmHg.

Patients suffering from any other disease (cardiac, renal, hepatic etc) other than HTN were excluded from study (exclusion criteria).

BP measurement: both systolic and diastolic BP were measured twice by mercury sphygmomanometer half an hour apart and then averaged.

Anthropometric measurements: height and weight were measured and BMI and WHR were calculated by formulae. BMI= Weight in Kg/ height in cm^2 WHR= waist in cm/height in cm

Measurement of Hematocrit: traditionally it is determined by measuring the height of red cell column in microhematocrit tube following centrifugation. Automated analyzer (Advia) calculates the Hct by multiplying the red cell count and the mean red cell volume, both of which are measured directly by machine. Normal value: 38-42%

Estimation of hemoglobin: is done traditionally using the cyanomethemoglobin method. To measure the Hb concentration, a lysing agent is added to a sample of diluted blood, which disrupts all red cells in the sample and released Hb, which is then converted into Cyanomethemoglobin and the concentration is read by spectrophotometer with the wavelength set at peak absorbance of cyanomethemoglobin. The concentration of Hb is then calculated from the optical density of the solution. Hb concentration is 1/3rd of Hct and is reported as grams/dL of blood. Normal values: 12-15 g/dL

Quantitative Determinations of TG and LDL were performed by enzymatic in vitro test in human serum on Roche cilinical chemistry analyzer using commercially avaialbale GPO-PAP and LDL kit respectively

Values NCEP[19]	**TG mg/dL**	**LDL mg/dL**
Normal	<150	<100
Borderline:	>150-199	130-159
High:	>200-499	> 160

Measurement of Aldosterone: was done by ^{125}I radioimmunoassay, based on aldosterone specific antibody immobilized to the wall of polypropylene tube (ELISA)

Normal value: Standing: 4-31 ng/dL, Recumbent: 1-16 ng/dL

Ethical consideration: Written consents of subjects were taken and study was approved by Board of advanced studies of Karachi University.

Results

The mean Hct level of HTN stage-I was significantly higher ($p<0.05$) than the mean of HTN stage-II (44.7±5.25 vs 42.0±3.83; p=0.014) as well as control and pre-HTN groups, as shown in Table 1. Hct level showed significant positive correlations with BMI, TG, K+ and aldosterone, in both stages-I and II of HTN (Table 2)

The mean Hb value was significantly higher in HTN stage-I (15.4±2.20) as compared to control, pre-HTN group ($p<0.001$), and HTN stage-II group i.e. 13.2±1.56 ($p<0.005$) as shown in Table 3. Significant correlation was seen between Hb level and systolic BP only in HTN stage-I, whereas no positive relation was observed with diastolic BP. Hb was positively correlated to systolic BP and WHR in both HTN stages -I and II (Table 2).

The serum TG level was on higher side in HTN stage-I (161.8±79.9) and II (166.6±66.7) as compared to control and pre-HTN groups. The mean LDL level was 106.5±30.7, 105.6±32.7, 116.4±32.9, and 103.7±29.2 in four groups respectively, the highest level being in HTN stage-I (Table 4).

The values of serum K+ were insignificant among four groups: 4.5±0.43, 4.47±0.42, 4.26±0.51 and 4.41±0.45 respectively. The mean aldosterone level was on higher normal side in HTN stages-I and II, i.e. 12.41±5.72, and 2.05±6.84 (Table 4).

Statistical analysis: Data was analyzed by SPSS version 15. The variables were presented as Mean ± standard deviation. Analysis of variance was performed to compare four study groups and LSD test was applied to compare pair-wise group.

Test of linear correlation was applied to asses relationship of different variable with systolic and diastolic pressure. Coefficient correlations of parameters were carried out with each other and within each of the four groups to identify the association of different variables with one another in different stages of hypertension. P value is taken as significant at <0.05.

Discussion

One of the objectives of evaluation of patients with documented HTN is to reveal identifiable causes of high BP.

The purpose of this study was to explore the association of some of the environmental and endogenous risk factors and to identify their correlation in different stages of HTN in Pakistani population, whose 18% adults suffer from this disease.[20] The BP level attributed to HTN in most of the studies done in Pakistan was >140/90 mmHg, but in this study subjects were classified into three groups

of HTN including the pre-HTN stage with high normal BP.

Table 1: Comparison of mean Hematocrit (Hct) among study groups (n=276)

S #	A	B	C	D
Group	Control (n = 75)	Pre HTN (n = 55)	HTN stage-I (n = 70)	HTN stage-II (n = 76)
Mean± SD	40.3 ± 4.30	40.4 ± 3.50	44.7 ± 5.25	42.0 ± 3.83
Pair-wise comparison statistical significance	-	v/s A=0.929	v/s A=0.001*	v/s A=0.381
	-	v/s C=0.003*	v/s D=0.014*	-
	-	v/s D=0.474	-	-

* The mean difference is significant at the 0.05 level.

Table 2: Coefficient correlation of HCT and Hb with other variables in HTN stage-I and II

Variable	SBP	BMI	WHR	TG	Serum K+	Aldosterone
Hemoglobin						
HTN stage-I	.396**	.077	.246**	.012	.116	.134
HTN Stage-II	.450**	.072	.236**	.073	.171	.052
Hematocrit						
HTN stage-I	.097	.298**	.220	.362**	.266*	.615**
HTN stage-II	.082	.263**	.247*	.340**	.294**	.533**

** Significant at the 0.01 level (2-tailed)
* Significant at the 0.05 level (2-tailed)

Table 3: Comparison of mean Hemoglobin (Hb) among study groups (n = 276)

S #	A	B	C	D
Group	Control (n = 75)	Pre HTN (n = 55)	HTN stage-I (n = 70)	HTN stage-II (n = 76)
Mean± SD	12.3 ± 1.84	12.7 ± 1.97	15.4 ± 2.20	13.2 ± 1.56
Pair-wise comparison statistical significance	-	v/s A=0.352	v/s A<0.001*	v/s A=0.004*
	-	v/s C<0.001*	v/s D=0.024*	-
	-	v/s D=0.08	-	-

* The mean difference is significant at the 0.05 level.

Table 4: comparison of mean of different variables among study groups (Mean±SD)

Group	Control	Pre-HTN	HTN Stage-I	HTN stage-II
BMI	24.9±3.77	26.4±4.47	28.4±4.53*	26.6±5.33
WHR	0.90±0.06	0.94±0.07	0.99±0.05*	0.99±0.06
TG	134.6±60.3	136.1±62.2	161.8±79.9*	166.6±66.7
LDL	106.5±30.7	105.6±32.7	116.4±32.9*	103.7±29.2*
Serum K+	4.5±0.43	4.47±0.42	4.26±0.51	4.41±0.45
Aldosterone	9.17±3.49	8.76±3.31	12.41±5.72*	12.05±6.85

* The mean difference is significant at 0.05 level

Most of the participants were educated and belonged to lower middle class; detail of subject profile has been published previously. [21]

Hct and HTN are intricately correlated, such that lowering the Hct can directly decrease BP by altering total peripheral resistance. Blood viscosity can therefore be employed as a very useful and sensitive indicator of BP. [22] The mean Hct level of HTN stage-I was significantly higher than the mean of all other groups; whereas the mean Hb level was also significantly higher in HTN stage-I (15.4±2.2) as compared to control and pre-HTN groups ($p<0.001$) and HTN stage-II group ($p<0.05$). Significant correlation was seen between Hb level and systolic BP both in HTN stage-I and II.

The quantity and distribution of body fat was assessed by two indicators, BMI and WHR in this study, as WHR is regarded as three times better predictor of risk of heart attack as compared to BMI.[23] This study confirmed that percentage of overweight and obese persons, has risen sharply in Pakistani general population even in middle and lower classes. In this study 69 % subjects in control group, 80% in pre-HTN, 90% in stage-I and 76 % in stage-II were overweight and obese, which is contrary to previously reported data showing 25% overweight and 10.3% obese people in our population. [24]

Both Hct and Hb were positively correlated to BMI in HTN stage-II, and to WHR in HTN stage-I and II. This suggests a link between these hematologic parameters and obesity, as strongly claimed by a latest study that among classical cardiovascular risk factors, WHR is closely related to blood viscosity. [25] Another study supported our finding in which untreated hypertensive patients had higher BMI, Hct and BP in both sexes. [26] A study on Iranian women reported that obese women have greater iron stores in terms of serum ferritin, Hb and Hct concentration than do non-obese women and are more prone to develop HTN. [27]

A correlation between Hb and IR was found in non-smokers in a study which also showed association of Hb with other components of IR such as BMI, WHR, lipid profiles, and systolic BP, which is consistent with our findings.[28] Our results thus provide support for a relationship between IR and hematological parameters such as Hb and Hct. Previously a study revealed that high erythrocyte count and Hb are associated with obesity and HTN [9] and another study documented that with treatment of anemia, increased Hct was followed by increased blood viscosity together with a rise of BP. [29]

Hyperviscosity has been found to be related to not only HTN but also IR, metabolic syndrome, severe obesity and peripheral atherosclerosis in adults.[10] The importance of TG as an independent risk factor has been reported by several studies, as TG rich lipoproteins penetrate endothelial cell layer, forming foal cells, a hallmark of atherosclerosis, the process especially enhanced in low shear stress areas of arteries.[30] IR and hyperinsulinemia have been observed in over 70% of non-obese, non-diabetic subjects with essential HTN, suggesting the resistance results from endothelial dysfunction and impaired endothelial dependent vasodilation.[31] A study confirmed that insulin was related to BMI and aldosterone in both normotensive and hypertensive subjects. [32] This study reported significant correlation of Hct with hormone aldosterone in both HTN stage-I and II for the first time.

The interrelationship among these factors as evident by this study, may tentatively suggest the possible sequence of mechanisms causing HTN as: visceral fat accumulation (TG, LDL) in upper abdomen impairs endothelial function, leading to a decrease in responsiveness of cells to insulin (IR) as well as decrease K+ entry into the cells, increasing plasma K+ level, which is a very strong stimulus for secretion of aldosterone, and needs to increase only 1 meq/L to stimulate its release from adrenal cortex. The aldosterone in turn, causes sodium and water retention. High Hct further aggravates the condition by increasing peripheral resistance and Hb impairs vasodilation by affecting NO availability; thus all these factors cumulatively result in HTN

Conclusion

Patients with a new diagnosis of HTN should be evaluated with a history, physical examination and the initial workup which should include the simple and cost effective tests, that provide an insight to the possible treatable causes of high BP and assessment for the presence of target organ damage. To promote primary prevention of HTN, identification and monitoring of increase in weight, lipid profile, blood glucose level and other related factors in HTN-prone subjects are considered important to prevent Clustering of different risk factors.

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