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Original Research Article

Comparison of hematological parameters in primary hypertensives and normotensives of Sangareddy

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Abstract

Background: Hypertension is the major health problem throughout the world because of its high prevalence and its association with increased risk of cardiovascular diseases.

Aim: The aim of present study was to evaluate the hematological changes in primary hypertension in Sangareddy, Andhra Pradesh.

Materials and Methods: In the present study, a total of 100 patients diagnosed for primary hypertension and 100 normotensive subjects were included. All the participants after taking informed consent were subjected to detailed history and hematological analysis. Students-'t' test was used to find out the significance of differences. P values less than 0.05 was considered the level of significance.

Result: It was observed that the mean values of Hemoglobin, Erythrocyte count, Hematocrit, MCH and MCHC were increased in primary hypertension while, the mean levels of MCV were found to be lower in the hypertensive group when compared to normotensive subjects.

Conclusion: Hypertension has impact on hematocrit, hemoglobin, RBC count, WBC count and Platelet count which can be used for early detection of hypertensive prone individuals.

Keywords: Hematocrit(HCT), Hemoglobin(Hb), Red Blood Cell(RBC), White Blood Cell(WBC).

1.Introduction

Hypertension is the major health problem throughout the world because of its high prevalence and its association with increased risk of cardiovascular diseases[1]. Prospective studies with varying lengths of follow-up have identified variables that seem to be altered in normotensive individuals whose blood pressures fit the clinical definition of "hypertension" during the follow-up period[2].

A growing number of variables are being identified in population cross-sectional studies or in laboratory studies that are related to mechanisms involved in blood pressure control. Although these studies increase knowledge of the pathophysiology of blood pressure control, it is important to differentiate between factors that are altered before the actual blood pressure increase and factors that respond to the blood pressure changes[2].

The situation in India is more alarming. Hypertension is a major public health problem in India and in other developing countries. This is obvious from several Indian urban and rural studies. The various studies estimated a prevalence rate of hypertension among urban population ranging from 1.24% in 1949 to 36.4 % in 2003 and for rural people from 1.99% in 1958 to 21.2% in 1994. However differential rates are due to different cut off marks in determining the level of hypertension and also differing age groups constituting the study population[3]. It has been predicted that by 2020, there would be a 111% increase in cardiovascular deaths in India[4].

The objective of the present study will be that it is useful in predicting the risk factors of cerebrovascular diseases through the regular investigations done routinely. Identification of these high-risk patients may allow an earlier introduction of antihypertensive treatment and for correction of the cardiovascular risk factors to impair the progression or to induce the regression of silent vascular damage before a clinical event develops by instructing change in the lifestyle or prescribing medications or both to prevent or to delay the occurrence of CVD.

The aim of the present study is to calculate and analyze the relation between blood pressure (systolic & diastolic) and different hematological and biochemical parameters in primary hypertensives and normotensives in Sangareddy and nearby villages.

2. Materials and Methods

Present study is conducted at MNR Medical College and Hospital, Sangareddy after taking institutional ethical clearance. Informed, written consent is taken from all the participants. A total of 100 patients diagnosed as primary hypertensives based on WHO criteria were included in the study. Age and Sex matched 100 normotensive subjects were taken as control.

2.1 Equipment

Sphygmomanometer, Stethoscope, Sterile apparatus for blood sample collection, Vaccutainer for sample preservation, Semi-autoanalyser.

2.2 Subjects

100 Primary Hypertensive patients as case group and 100 normotensives as control group.

2.2.1 Inclusion Criteria:

Recently detected (below 3 months) Primary hypertensives.

2.2.2 Exclusion Criteria

Subjects with a history of atherosclerotic disease(myocardial infarction or stroke in the previous 6 months), congestive heart failure, diabetes, Primary hypertension duration more than 1 year irrespective of whether under medication or not, Secondary hypertension, any Chronic diseases, under any medication which are known to alter the parameters.

2.2.3 Population where subjects will be selected from: Sangareddy and nearby villages.

2.2.4 Male/Female ratio of subjects: equal (i.e., 1:1).

2.2.5 Age range of subjects: 30 to 60 years.

2.2.6 Compensation (if any) that will be offered to subjects: -Nil-

2.3 Description of experiment, data collection and analysis: 100 hypertensive males and females aged 30 to 60 years and similar numbers of normotensives are selected as control randomly. The selection is from the population of Sangareddy and nearby villages with all its socio-economical and genetic variabilities. Extreme care is taken in the random selection of hypertensive and control groups to ensure that they represented a broad cross sectional coverage of all population. The control group consists of healthy volunteers who are not taking any hormones or drugs known to affect plasma lipid levels.

The following information was collected from each subject through a validated questionnaire administered by the volunteers: name, age, sex, occupation, weight, height, history of diabetes, family history of hypertension, past history of any examination of blood pressure and hypertension, or any it's complications, any symptom referable to target organ dysfunction, previous an present treatment profile, and addictions.

Hypertension is considered to be present if subjects met the criteria of Systolic pressure of 140mmHg and above and Diastolic pressure of 90mmHg and above on two occasions[5].

Blood pressure was recorded in the sitting position for the right arm to the nearest 2mmHg using the Mercury Sphygmomanometer (Diamond Deluxe BP apparatus, Pune, India). Blood pressure is measured for each participant, using the palpatory and auscultatory methods with a standardized calibrated mercury column type sphygmomanometer and an appropriate sized cuff encircling at least 80% of the arm in the seated posture, with feet on the floor and arm supported at heart level. Following a standardized protocol, three separate measurements with interval of 5minutes are recorded and the average of the three measurements after proper rest and due explanation to the examined participants about the objective of the study. Systolic BP is the point at which the first of two or more sounds is heard (Phase I) and Diastolic BP is the point before the disappearance of sounds (Phase V)[6].

Blood samples are obtained after an overnight fasting from midcubital vein in antecubital fossa making the subject to sit comfortably in a chair. Through a sterile DISPOVAN syringe under sterile precautions, about three milliliters of blood is collected in EDTA coated vaccutainers. The sample is then analyzed for the said hematological parameters using *MISPA EXCEL* semiautonomous analyzer.

The readings for the values of RBC Count, Hemoglobin, Hematocrit, Leucocyte count and Thrombocyte count are taken and noted. The erythrocyte indices i.e., MCV (Mean Corpuscular Volume), MCH (Mean Corpuscular Hemoglobin)

and MCHC (Mean Corpuscular Hemoglobin Concentration) are calculated from the known values of Hemoglobin, RBC count & Hematocrit as follows:

$$MCV = \frac{\text{Hematocrit}}{\text{RBC count}} \times 10\ (\mu m^3)$$

$$MCH = \frac{\text{Hemoglobin}}{\text{RBC count}} \times 10\ (pg)$$

$$MCHC = \frac{\text{Hemoglobin}}{\text{Hematocrit}} \times 100\ (\%)$$

The readings for Leucocyte count and Thrombocyte count are also noted.

2.4 Statistical Analysis

The mean levels of various hematological parameters were correlated. Student-'t' test was used to find out the significance of differences. P values less than 0.05 were considered the level of significance.

3. Results

All values were expressed as mean ± S.E. Statistical significance of differences between control and study groups were evaluated by student's "t" test. A p-value of <0.05 is considered to be statistically significant and p-value of <0.01 is considered to be more significant.

Table 1: The mean hematological values of the study

Parameter	Normotensive mean ± SD	Hypertensive mean ± SD	P value	Significance
Hemoglobin	10.90±1.25	11.80±1.68	<0.01	HS
RBC Count	3.88±0.36	4.14±0.54	<0.01	HS
Hematocrit	31.44±1.81	32.36±3.21	<0.05	S
WBC Count	6628±1335	7704±1635	<0.01	HS
Thrombocyte count	2.83±0.80	3.47±0.89	<0.01	HS
MCV	81.62±7.96	78.82±8.32	<0.05	S
MCH	28.15±2.65	28.60±3.12	>0.05	NS
MCHC	34.65±3.26	36.54±4.27	<0.01	HS

(Mean ± SD) of hematological parameters of normotensive controls and hypertensive groups

The mean values of Hemoglobin, Erythrocyte count, Leucocyte count and Thrombocyte count are found to be higher in hypertensive group with high significance.

The mean value of Hematocrit is significantly higher in hypertensive group when compared to normotensives.

The mean value of MCV is significantly lesser in hypertensive group.

The mean value of MCH is higher in hypertensive group with no significance.

The mean value of MCHC is significantly more in hypertensive group.

4. Discussion

4.1 Hemoglobin & Erythrocyte count

In the present study, the mean levels of Hemoglobin and Erythrocyte count were found to be significantly higher in the hypertensive group. The mean levels of Hemoglobin and Erythrocyte count in hypertensives were (11.80±1.68), (4.14±0.54) and in controls were (10.90±1.25), (3.88±0.36).

From these findings it can be concluded that in primary hypertension, the mean hemoglobin and erythrocyte count are increased significantly.

These findings are similar to the earlier findings by Giacomo *et al*[7], Massimo *et al*[8], Dan *et al*[9] and Al-Muhana *et al*[10].

They stated that two ionic systems are involved in cell volume regulation, namely, a loop diuretic-sensitive Na+-K+ symport and intracellular calcium, have also been reported to be altered in hypertension. Increasing intracellular calcium with ionophores makes red blood cells shrink their volume[7].

Other results also show positive correlation between blood hemoglobin and blood pressure in hypertensives.[7,9,10] High blood pressure could theoretically cause high Hematocrit by, for instance, inducing hemoconcentration through increased transcapillary filtration of plasma. No research data are available in support of the hypothesis that an increase in blood pressure is followed by an increase in hematocrit. If high blood pressure were the only cause of high hematocrit in the hypertensive group, a reasonable expectation is that hematocrit would have been lowered at least to some degree by effective antihypertensive treatment. The lack of such an effect in hypertensive individuals indicates the unlikelihood that high hematocrit is merely secondary to high blood pressure. Alternative possibilities are that hematocrit contributes to the regulation of blood pressure or that some other factors are responsible for parallel changes of hematocrit and blood pressure. The role of other (possibly dietary) factors not considered in the present study cannot be excluded[8].

4.2 Hematocrit

In the present study, the mean levels of Hematocrit were found to be significantly higher in the hypertensive group. The mean levels of

Hematocrit in hypertensives were (32.62±3.93) and in controls were (31.54±2.00).

From the above findings it can be concluded that increased hematocrit level is seen in primary hypertensives.

This is similar to the findings of Giovanni de Simone[11], Massimo *et al*[8], Dan *et al*[9] and Al-Muhana *et al*[10].

The possibility that hematocrit has a direct role in the regulation of the blood pressure is supported by experimental and clinical observations. In patients with different forms of anemia, a significant increase of total peripheral resistance and arterial pressure and at times development of hypertension may occur when low hematocrit is increased by transfusion of packed red blood cells or by erythropoietin administration. Results of the previous studies indicate that a 10-unit increase in hematocrit (e.g., from 35% to 45%) would be associated with an increase of 4-6 mm Hg in arterial pressure and with a twofold increased risk of hypertension[8].

Reasonable mechanisms underlying the association between hematocrit and blood pressure are the relations of hematocrit with whole blood viscosity, of whole blood viscosity with peripheral resistance, and of peripheral resistance with blood pressure. It has been proposed that with treatment of anemia, cessation of vasodilation (previously present because of tissue hypoxia) and increased blood viscosity, both resulting from the therapeutic increase in hematocrit, account for the increased peripheral resistance with rise of blood pressure observed. It seems unlikely that a hypoxia related mechanism can explain the association between hematocrit and blood pressure in general populations. Therefore, the greater blood viscosity caused by higher hematocrit and the consequent increased resistance to blood flow appear the most reasonable causes underlying the association between hematocrit and blood pressure in the present study.

High hematocrit in hypertension could reflect a true increase in red blood cell mass as well as hemoconcentration caused by a reduction in plasma volume. Plasma volume in established essential hypertension is reported to be normal, low, or also high in some individuals. This might lead to the conclusion that hypertensive individuals have a continuum of plasma volume values not different from that of nonhypertensive individuals or that low, normal, or high plasma volumes reflect different forms of essential hypertension or different stages of the disease. Data from the present report cannot rule out the possibility that high hematocrit is characteristic of hypertensive people with reduced plasma volume[8].

4.3 Mean corpuscular volume

The mean levels of Mean Corpuscular Volume (MCV) were found to be significantly higher in the hypertensive group. The mean levels of MCV in hypertensives were (81.95±9.73) and in controls were (87.56±7.47).

The MCV appears to be inversely related to Systolic and Diastolic Blood Pressures. The following model is suggested by these results:

The above findings show that there is decreased Mean Corpuscular Volume (MCV) in primary hypertensives.

These results are consistent with the studies reported by Dan *et al*[9], Giacomo *et al*[7] and Al-Muhana *et al*[10]

With the above results, the following hypothesis can be made to show how the increased blood pressure leads to decreased MCV:

Viscosity affects peripheral resistance to blood flow, and peripheral resistance affects DBP. At high RBC levels, MCV may be down regulated. This may lower whole blood viscosity and partially reduce DBP without compromising flow[9].

1. Because essential hypertension is primarily a derangement of peripheral vascular resistance and because DBP is a more specific measure of overall resistance to blood flow than SBP, blood characteristics that influence viscosity will be more strongly related to DBP than to SBP.
2. The impact of an increase in relative red cell mass is to increase whole blood viscosity, primarily by increasing the number of particles per unit volume of blood (RBC), and thereby increase peripheral resistance to blood flow.
3. To maintain blood flow in the face of increased peripheral resistance, blood pressure increases.
4. The deleterious consequence of increasing pressure, presumably to maintain blood flow is partially compensated for by a concomitant decrease in red cell volume, thus attempting to counteract the viscous effects of a larger relative red cell mass (i.e., count) with smaller cell size characteristics.[20] Giacomo *et al* investigated three hematological indexes-MCV, platelet volume and RBC count investigated and found MCV to decreased in hypertensives.
5. It is interesting to note that two ionic systems involved in cell volume regulation, namely, a loop diuretic-sensitive Na+-K+ symport and intracellular calcium, have also been reported to be altered in hypertension. Increasing intracellular calcium with ionophores makes red blood cells shrink their volume[7].

4.4 Leucocyte Count

In the present study, the mean levels of Total Leucocyte Count were found to be significantly higher in the hypertensive group. The mean levels of Total Leucocyte Count in hypertensives were (7704±1635) and in controls were (6628±1335).
The above findings show that there is increased WBC count in primary hypertensives.

The results are similar to the findings reported by Chong Do Lee[12] Jeremy *et al*[13], Benjamin *et al*[14], Sun *et al*[15], Dong-Jun *et al*[16] and Al-Muhana *et al*[10].

Although an elevated WBC count is considered a risk marker for cardiovascular disease incidence and mortality, there has been little research on this relation in Indians. The major finding was that elevated WBC count is directly associated with hypertension and also with the risk of coronary heart disease and stroke incidence and mortality from cardiovascular disease. It is plausible that an elevated WBC count may enhance atherogenesis. Granulocytes and Monocytes are believed to be involved in the pathogenesis of atherosclerosis. Monocyte-derived macrophages produce oxidants that can induce endothelial cell injury and subsequent thrombus formation. Activated WBCs also reflect the inflammatory activity of atherosclerosis that perpetuates vascular injury and tissue ischemia. Some studies have reported that WBC count is also associated with several cardiovascular disease risk factors. These findings include positive associations with body weight, systolic blood pressure, fasting glucose level and negative associations with high density lipoprotein cholesterol level[12].

As cytokines are potent inducers of leucocyte differentiation, they speculated that an activated cytokine system might lead to elevated leucocyte levels. Furthermore, activated differentiated leucocytes can produce more cytokines. There is a possibility that hormones such as cortisol or insulin, which are known to be increased in metabolic syndrome, then stimulate leucocyte propagation. Some data are available on the association between differential leucocyte counts and coronary heart disease[16].

4.5 Thrombocyte count

In the present study, the mean levels of Thrombocyte Count were found to be significantly higher in the hypertensive group.

The mean levels of Thrombocyte Count in hypertensives were (3.47±0.89) and in controls were (2.83±0.80).

The above findings show that there is increased platelet count in primary hypertensives.

These results are significantly consistent with the studies reported by Giacomo *et al*[7], Khandekar *et al*[17], Paul *et al*[18] and Al-Muhana *et al*[10].

The increase in platelet consumption at the site of the coronary atherosclerotic plaque causes larger platelets to be released from the bone marrow. Because larger platelets are haemostatically more active, the presence of larger platelets is probably a risk factor for developing coronary thrombosis and MI. Platelet count can easily be done during routine hematological analysis, it is also generated as a byproduct of automated blood counts[17].

The pathophysiology of arterial thrombosis is complex, with many genes dictating physiologic and biochemical traits that modify one another to increase or decrease the risk for developing adverse clinical outcomes. Environmental factors also impinge on the risk, as do age and gender. The position of platelets in acute coronary syndromes is well established and is grounded in physiologic, pathologic, and clinical studies. Platelet deposition onto the sub-endothelium is proportional to the shear rate, such that platelets play a particularly important role in arterial thrombosis. Upon arterial plaque rupture, Von-Willebrand Factor (VWF) molecules are rapidly localized to the sub-endothelium and the initial platelet contact with the wound is a tethering of platelets to this insoluble form of VWF. The glycoprotein (GP) GPIbα subunit of the GPIb-IX-V complex mediates this tethering to VWF, resulting in a slower platelet velocity, which in turn permits platelet GPVI to bind to collagen. Signaling between and through GPIbα and GPVI causes platelet activation, resulting in secretion, firm platelet adhesion through activated integrins: α2β1 binding to exposed collagen and GPIIb-IIIa (integrin αIIbβ3) binding to VWF and fibrinogen. An expanding thrombus ensues when platelets aggregate via the intercellular bridging of fibrinogen and VWF binding to the activated conformation of GPIIb-IIIa. Blood flow ceases when an occlusive platelet plug forms[18].

5. Summary and Conclusion

To summarize, in the present work the variables found significant in this study can be suggested as the predictors of hypertension.

In the present study, the mean values of the parameters of Hemoglobin, Erythrocyte count, Hematocrit, MCH and MCHC are increased in primary hypertension; while, the mean levels of MCV were found to be lower in the hypertensive group.

The present study reports, in a general population sample, an independent significant association between Hemoglobin, Hematocrit, RBC Count, and prevalence of hypertension and a positive relation between Hemoglobin, Hematocrit, RBC Count and blood pressure. Hematocrit is, on average, high in hypertensive individuals despite reduction of blood pressure suggesting that high hematocrit in hypertension is not secondary to high blood pressure.

The increase in platelet consumption at the site of the coronary atherosclerotic plaque causes larger platelets to be released from the bone marrow. Because larger platelets are haemostatically more active, the presence of larger platelets is probably a risk factor for developing coronary thrombosis and MI.

Because essential hypertension is primarily a derangement of peripheral vascular resistance and because DBP is a more specific measure of overall resistance to blood flow than SBP, blood characteristics that influence viscosity will be more strongly related to DBP than to SBP. The impact of an increase in relative red cell mass is to increase whole blood viscosity, primarily by increasing the number of particles per unit volume of blood (RBC), and thereby increase peripheral resistance to blood flow. To maintain blood flow in the face of increased peripheral resistance, blood pressure increases. The deleterious consequence of increasing pressure, presumably to maintain blood flow is partially compensated for by a concomitant decrease in red cell volume, thus attempting to counteract the viscous effects of a larger relative red cell mass (i.e., count) with smaller cell size characteristics. It is interesting to note that two ionic systems involved in cell volume regulation, namely, a loop diuretic-sensitive Na+-K+ symport and intracellular calcium, have also been reported to be altered in hypertension. Increasing intracellular calcium with ionophores makes red blood cells shrink their volume.

From the above study it can be concluded that in patients of primary hypertension, significant changes are seen in hematocrit, hemoglobin, RBC count, WBC count and Platelet count which can be used for early detection of hypertensive prone individuals.

Conflict of Interest: Authors declare they have no conflict of interest.

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