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COMPARATIVE CHANGES IN HEMORHEOLOGIC PROPERTIES OF HYPERTENSIVE AND NORMOTENSIVE ADULTS

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ABSTRACT
In Scientific term, hemo-rheology describes the rate of material flow and movement through the blood and vascular system. It is a feature of the circulatory system that reportedly varies across humans, and may be dependent on disease states, such as hypertension. Current study was therefore devised to compare and contrast selected hemo-rheological variables in hypertensive and normotensive adult humans. One hundred and forty (140) humans, comprising of seventy (70) hypertensive and normotensive subjects each were ethically recruited from the University of Benin staff and students community. Haven established their health status via questionnaire and history taking, subjects were then grouped into two based on their blood pressures (BP); Group 1 [Normotensives, BP < 120mmHg/80mmHg] and Group II [Hypertensives, BP > 140mmHg/90mmHg]. After obtaining their anthropometric parameters (weight, height and BMI), blood samples were then obtained from subjects and assayed for selected hemo-rheologic parameters [pH, Whole Blood Viscosity (WV), Plasma Viscosity (PV), Plasma Fibrinogen Concentration (PFC), Packed Cell Volume (PCV) and Euglobinlysis time (ELT)]. Upon statistical comparison (using the student t-test), study found a significant increase in all but WV, pH, PV and PCV. These variables however proved significant across gender line, returning a statistically significant increase ($p < 0.05$) in hypertensive males than females. Hemo-rheological changes can therefore be associated with hypertensive state.

KEYWORDS: hemo-rheology, Hypertensives, Normotensives.

INTRODUCTION

One of the most important markers of cardiovascular risk status is hypertension. Proper management as such is thus essential for the prevention of cardiovascular complications. In recent times, Hemorheological variables have been reported to be linked with hypertensive states, even though it is still not known if hemorheological abnormalities are the cause or the result of systemic arterial hypertension.[1&2] Also, a strong positive correlation reportedly exists between the human blood pressure and hematocrit values[2], with whole blood viscosity, plasma viscosity and red blood corpuscular aggregations having huge tendencies to increase with decreasing erythrocyte deformability in hypertensives.[3]

In a similar vein, by altering hemodynamic resistance, hemorheological changes have been shown to increase arterial blood pressure[4], while improving generic sensitivity to disturbances in living organism.[5]

In Caucasians, several studies posit that haemorheologic variables are likely to increase in hypertensive state with accompanying increases in plasma and whole blood viscosity.[2,5] This may likely cause an increase RBC aggregation with a preponderant increase in PCV levels, whilst decreasing RBC deformability[5], increasing the concentrations of plasma protein; globulin and fibrinogen[6] with variable changes in the levels of haematocrit.[7] These changes reportedly predispose hypertensives to increased viscosities with associated cerebrovascular and cardiovascular co-morbidity and mortalities.[8]

Particularly, Africans are reportedly susceptible to hypertension with its associated complications.[4,9] However, rheological reports posit great changes in Nigerian hypertensives, even though this may be relatively scanty. In a recent survey, a significantly higher fibrinogen concentration, relative plasma viscosity and whole blood relative viscosity have been found in hypertensives Nigerians as against those that are normotensive.[5] These could be attributable to a significantly hyped fibrinogen levels reportedly seen in hypertensive humans.[9]

Though, little or nothing is known about gender variations in haemorheological variables amongst hypertensive Nigerians, research in this area has becomes imperative, considering that gender changes in rheological variables are known to be present in healthy African normotensives[10], and may be influential in thrombo-embolism with recourse to unfavourable prognostic measures.[11]

Aim of Study

Current study was designed to evaluate the differences in hemorheological properties of normotensive and hypertensive humans. Specifically, study comparatively investigated the differences in selected hemorheological parameters in male and female hypertensives, irrespective of their age

MATERIALS AND METHOD

Humans

One hundred and forty (140) humans, comprising of seventy (70) hypertensive and normotensive subjects each were ethically recruited from the staff and students community of the University of Benin, Benin City, Edo State, Nigeria.

Reagents and Anti-Coagulants

1. 10g of dipotassium salt dissolved in 100ml of distilled water. 3.8% sodium citrate dissolved in 100ml of distilled water.
2. 0.0025M $CaCl_2$ (2.77g of anhydrous grade $Cacl_2$ reagent dissolved in clean distilled water, and made up to 1L, this solution was refrigerated at 4^0C).
3. Dilute acetic acid (13.5ml of 1% v/v into 1000ml distilled water thoroughly mixed and stored in the fridge).
4. Borate buffer (9.0g NaCl plus 1.0g of sodium borate in 1L of volumetric flask filled with distilled water).

Questionnaire

Using a carefully structures questionnaire, participants' health status was first ascertained, and their base line data (weight, Blood Pressure and BMI) status obtained. The questionnaire was structured to be void of unnecessary questions and/or ambiguity.

Ethical Clearance

Ethical clearance was obtained from the bio-research and ethics committee of the College of Medical Sciences, University of Benin, Benin City, Edo State, Nigeria.

Informed Consent

Participants' written and oral consent was also obtained before investigation.

Sample and Sampling Technique

Using the simple random sampling technique, a convenient, cross-sectional sample size of One hundred and forty (140) participants were drawn from within the staff and students community of the University of Benin, Benin City, Edo State, Nigeria. Obtained samples (participants) were then grouped into two based on their blood pressures (BP); Group 1 [Normotensives, BP < 120mmHg/80mmHg] and Group II [Hypertensives, BP > 140mmHg/90mmHg]

Selection Criteria

Subjects with known history of endocrine, metabolic, cardiovascular and any other medical disorders (as observed from questionnaire) were excluded from the study. Selection of subjects into groups (Normotensive and Hypertensive) was based on BP readings; Group 1 normotensive subjects (BP < 120mmHg/ 80mmHg), while Group 2 consisted BP >140mmHg/90mmHg)

Determination of BMI and BP

Subjects' heights were measured with the aid of a standometer, while obtaining weights with the weighing scale. Body mass index was thus calculated using the formula;

BMI= Weight (kg)/ Height (m^2).

Resting pulse rate and blood pressure were then measured in a sitting position using an omron sphygmomanometer twice and the average taken.

Blood Sample Collection

Soon after the obtaining participants' anthropometric parameters (with assistance from a trained phlebotomist), Blood samples were then collected form subjects' antecubital vein (at sitting position) in the cubital fossa. 9.5ml of blood was then taken from each person with minimum stasis using a 10ml syringe. Obtained blood was then dislodged into two 5ml specimen containers. 5ml of blood was added into a container containing 0.2ml of 10% ethylene diamine tetra acetic acid (EDTA) and immediately mixed. Next, 4.5ml of blood was added into another container containing 0.5ml of 3.8% sodium citrate and mixed immediately, then, kept in an ice filled container. Samples were immediately assayed for Whole Blood Viscosity (WV), Plasma viscosity (PV), Plasma Fibrinogen Concentration (PFC), Packed Cell Volume (PCV) and EuglobinLysis Time (ELT).

Determination of Whole Blood and Plasma Viscosity

(Method of Reid and Ugwu, 1987**)**

In principle, the test is based on the comparison of the flow rate of the whole blood/plasma and distilled water under equal pressure and constant temperature through capillary tube of equal bore and length, the result as expressed as whole blood/ plasma relative to that of water.

Instrument (capillary tub) was calibrated at room temperature against a controlled chamber used by Reid and Ugwu, (1987).[7 & 8] The measurement of the flow

rate of clean distilled water at room temperature was made by running 20 successive runs and the average was taken. The fluid (plasma or whole blood mixed with EDTA) to be tested was drawn up, cautiously excluding air bubbles in the vertical syringe until the plunger passed the 1.0 mark. The plunger was then completely withdrawn and immediately the lower meniscus fell to the 1.0 mark, a stopwatch was then started. The time required for 1.0ml of the fluid to drain down the syringe was taken. This was repeated twice on each sample and the mean flow rate was calculated. The whole blood relative viscosity and relative plasma viscosity was then calculated with the formula;
Whole blood relative viscosity / relative plasma viscosity = Test flow rate

Determination of Plasma Fibrinogen Concentration
(Ingram's clot weight method, 1961**)**
In principle, when calcium chloride is added to citrate plasma, this triggers off the intrinsic pathway of coagulation resulting in the formation of fibrin cloth, which can be collected, weighed and by calculating the weight of fibrinogen is obtained.[12]

To achieve this, 1ml of citrated plasma was pipetted into labeled test tube in water bath at 37^{o}C. Then 1ml of pre warmed 0.025M $Cacl_2$ was added into the test-tube and mixed. The mixture is left in the water bath for 30 minutes with an applicator stick dipped into the test tube so that clot can be wound around it. When all the adherent fibrin are removed from the applicator stick after washing 3 times with distilled water and then blot dry carefully with whittman filter paper. Then adherent fibrin is carefully removed from the applicator stick into clean-labelled Petri dishes and kept in an hot air oven to dry.

Calculation
<u>Dry weight x10/100ml</u>
Volume of plasma

Euglobin Lysis Time
(Methodology by Cecil Hougie 1967)
4½ ml of blood was collected plus 0.5ml of 1M sodium citrate into chilled 10ml centrifuge tube. The tube was placed in a refrigerator ice chambers at temp -20 to -10^{o}C for 2 minutes, then it was kept in ice chambers for 5minutes, and centrifuged at 2000rpm for 10 minutes. The Plasma was separated and kept in an ice chambers, plasma was then duplicated. 0.5ml of plasma was mixed with 9.5ml of dilute acetic acid, tube containing plasma and dilute acetic acid was refrigerated at 4^{o}C for 30 minutes and afterward centrifuged at 2000rpm for 10 minutes. Precipitant was formed, supernatant fluid was discarded, then 0.5ml of borate buffer was added to the precipitant and dissolved with a glass rod, the solution was placed in a water bath at 37^{o}C for 2 minutes. 1.5ml of 0.025M $Cacl_2$ was added to solution, and then the solution clotted. A timer was started immediately the clot was formed. The tubes were placed in warm water bath at 37^{o}C. The clot was observed at a regular interval of 2 minutes for lysis. At the point where the clot was completely lysed, the timer was stopped and the reading on the timer was noted.

Calculation
ELT= interval between clotting and complete lysis.
Fibrinolytic Activity (FA)= $10^6 / ELT^2$, ELT is in minutes.

Analytical Approach
Obtained data were analysed using appropriate descriptive statistics (mean, standard deviation). Were applicable, Student t-test and/or Analysis of variance (ANOVA) were used to obtain differences in mean between groups with $p < 0.05$ taken as statistically significant.

RESULTS
Table I: Comparative Average Differences in Hemorheological Variables of Hypertensives and Normotensives.

Hemorheological Parameters	Hypertensives	Normotensives	P-Value
SBP(mmHg)	142.89±1.61	120.67±1.09	p < 0.05
DBP(mmHg	92.72±1.19	78.87±0.87	p < 0.05
MAP(mmHg)	106.39±1.35	92.74±0.86	p < 0.05
PR(b/min)	83.31±0.83	73.77±0.43	p < 0.05
WEIGHT(kg)	80.47±0.95	75.81±1.13	p < 0.05
HEIGHT(m)	1.68±0.01	1.69±0.01	p > 0.05
BMI(kg/m2)	28.26±0.27	26.54±0.3	p < 0.05
pH	5.94±0.06	5.91±0.04	p > 0.05
SG	1.02±0	1.02±0	p > 0.05
PCV (%)	39.91±0.35	39.01±0.39	p > 0.05
WBV	7.25±0.19	6.74±0.15	p > 0.05
PV	2.61±0.04	2.44±0.39	p < 0.05
FA	9.74±0.48	24.84±1.3	p < 0.05
PFC(mg)	69.96±2.79	50.83±3.39	p < 0.05

Data is expressed as Mean ± SD. p < 0.05 = significant, p > 0.05 = Insignificant. SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, PR = Pulse Rate, BMI = Body Mass Index, SG = Specific Gravity, PCV = Packed Cell Volume, WBV = Whole Blood Viscosity, PV = Plasma Viscosity

Table II: Comparative Average Differences in Hemorheological Variables of Hypertensive and Normotensive Male Subjects.

Hemorheological Parameters	Hypertensive Male	Normotensive Male	P-Value
SBP(mmHg)	141.91±1.89	120.22±1.31	p < 0.05
DBP(mmHg	92.2±1.34	79.27±1.09	p < 0.05
MAP(mmHg)	106.03±1.42	92.78±1.05	p < 0.05
PR(b/min)	83.66±1.31	73.97±0.54	p < 0.05
WEIGHT(kg)	83.17±1.39	79.08±1.34	p < 0.05
HEIGHT(m)	1.7±0.02	1.72±0.01	p > 0.05
BMI(kg/m2)	28.26±0.38	26.84±0.36	p < 0.05
SG	1.02±0	1.02±0	p > 0.05
PCV(%)	41.57±0.37	40.51±0.47	p > 0.05
RWBV	7.51±0.29	6.29±0.18	p < 0.05
RPV	2.64±0.04	2.43± 0.39	p < 0.05
FA	10.69±0.73	23.52±1.44	p < 0.05
PFC(mg)	70.89±3.58	46.73±3.81	p < 0.05

Above table shows a clear significance in the SBP, DBP, PR, MAP and the BMI between the hypertensive and normotensive adult males. In the hemorheological parameters RWBV, RPV and PFC were significantly higher in hypertensive male subjects, although PCV was also higher among hypertensive male subjects but it was not significant. FA was significantly higher in male normotensives compared to male hypertensives. Data is expressed as Mean ± SD. p < 0.05 = significant, p > 0.05 = Insignificant.

Table III: Comparative Average Differences in Hemorheological Variables of Hypertensive and Normotensive Female Participants.

Parameters	Hypertensive Female	Normotensive Female	P-Value
SBP(mmHg)	143.86±2.61	121.18±1.81	p < 0.05
DBP(mmHg	93.24±1.97	78.42±1.41	p < 0.05
MAP(mmHg)	106.74±2.29	92.7±1.42	p < 0.05
PR(b/min)	82.97±1.03	73.55±0.68	p < 0.05
WEIGHT(kg)	77.77±1.13	72.15±1.66	p < 0.05
HEIGHT(m)	1.66±0.01	1.66±0.01	p > 0.05
BMI(kg/m2)	28.26±0.4	26.21±0.5	p < 0.05
PH	5.94±0.06	6±0.04	p > 0.05
SG	1.02±0	1.02±0	p > 0.05
PCV(%)	38.26±0.45	37.33±0.52	p > 0.05
RWBV	7.25±0.21	6.99±0.25	p > 0.05
RPV	2.57±0.07	2.45±0.07	p > 0.05
FA	8.79±0.6	26.37±2.26	p < 0.05
PFC(mg)	69.03±4.33	55.56±5.79	p > 0.05

Above table shows that among female subjects SBP, DBP, PR, MAP and BMI were significantly higher in hypertensive subjects. Among hemorheological parameters PCV, RWBV, RPV and PFC were higher in hypertensives but it was not significant, but FA was significantly higher in normotensive female subjects than hypertensive female subjects. Data is expressed as Mean ± SD. p < 0.05 = significant, p > 0.05 = Insignificant.

Table IV: Comparative Changes in Average Hemorheological Variables of Hypertensive Male and Female Participants.

Parameters	Hypertensive male	Hypertensive female	P-Value
BMI(kg/m2)	28.26±0.38	28.26±0.4	p > 0.05
RPV	2.64±0.04	2.57±0.07	p > 0.05
RWBV	7.52±0.29	7.25±0.21	p > 0.05
PCV	41.57±0.37	38.26±0.45	p < 0.05
FA	10.69±0.73	8.79±0.60	p < 0.05
PFC	70.89±3.58	69.03±4.33	p > 0.05

Above table shows that among hypertensive subjects there was significant increase in PCV and FA in male hypertensive subjects compared to their female counterpart, the other parameters had no significant difference. Data is expressed as Mean ± SD. $p < 0.05$ = significant, $p > 0.05$ = Insignificant.

Table V: Comparative Changes in Average Hemorheological Variables of Normotensive Male and Female Participants.

Parameters	Normotensive Male	Normotensive Female	p-value
BMI(kg/m2)	26.84±0.36	26.21±0.50	p > 0.05
RPV	2.43±0.06	2.45±0.07	p > 0.05
RWBV	6.29±0.18	7.25±0.21	p < 0.05
PCV	40.51±0.47	37.33±0.52	p < 0.05
FA	23.52±1.44	26.37±2.26	p > 0.05
PFC	46.73±3.80	55.56±5.79	p > 0.05

From above table, it is seen that among normotensive subjects there was significant increase in the PCV of male hypertensive subjects compared to their female counterpart, but RWBV was significantly higher in female normotensive subjects. The other parameters had no significant difference. Data is expressed as Mean ± SD. $p < 0.05$ = significant, $p > 0.05$ = Insignificant.

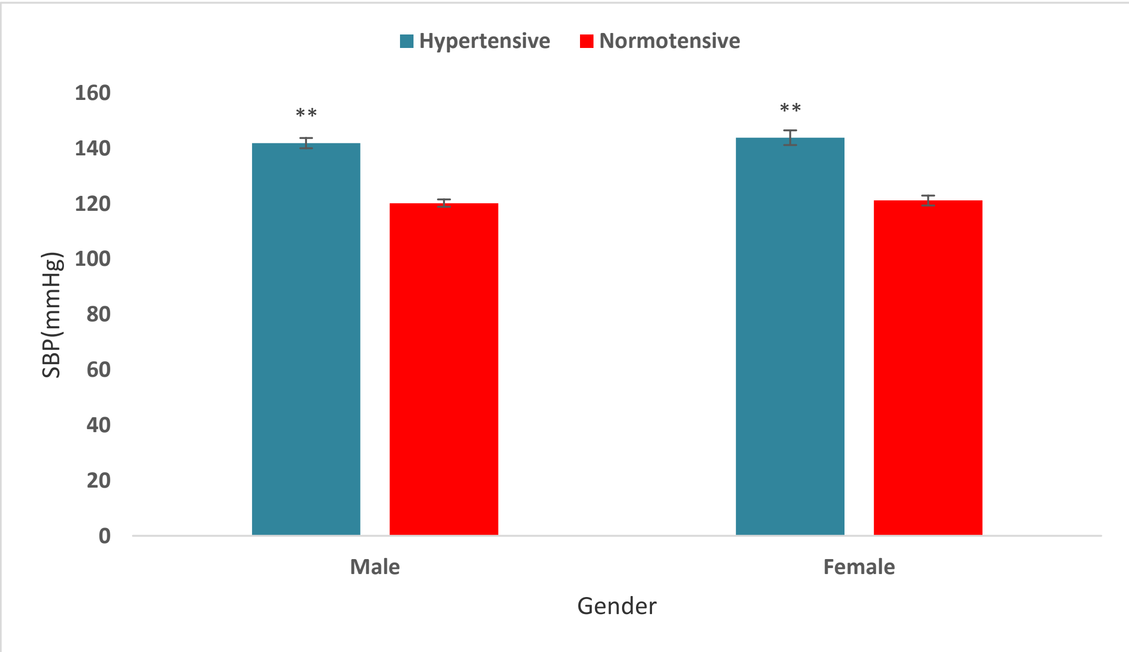

Figure 1: Comparative Changes in Systolic Blood Pressure of Normotensive and Hypertensive Male and Female subject

*** = significantly increased (at $p < 0.05$) compared to control (Normotensives)*

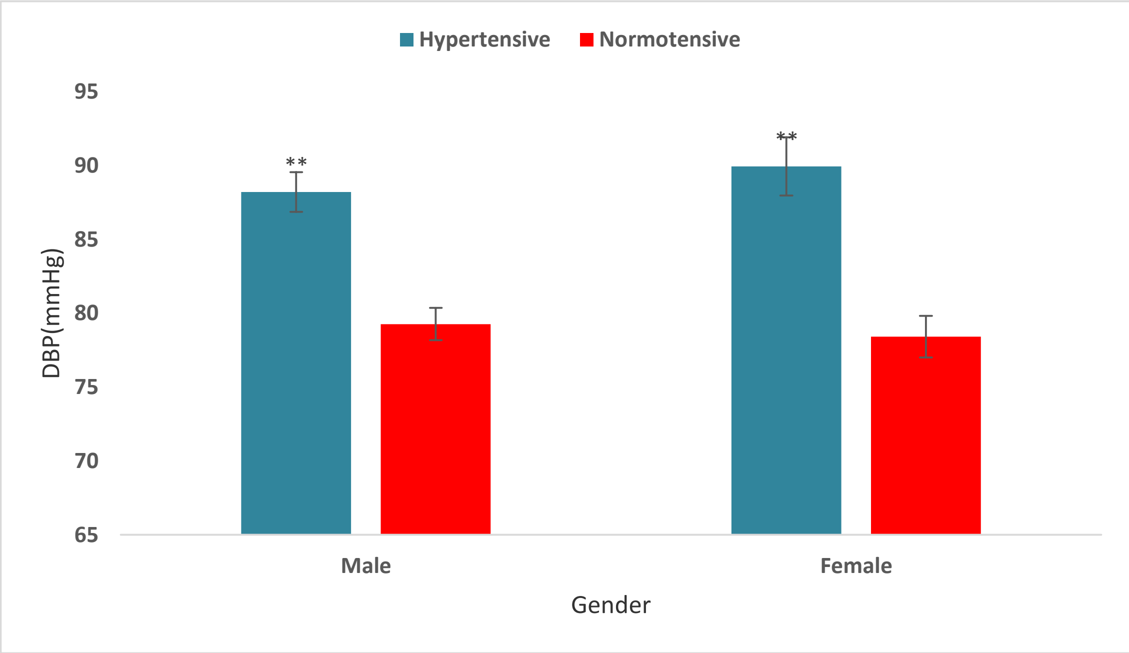

Figure 1I: Comparative Changes in Diastolic Blood Pressure of Normotensive and Hypertensive Male and Female subject.
*** = significantly increased (at p < 0.05) compared to control (Normotensives)*

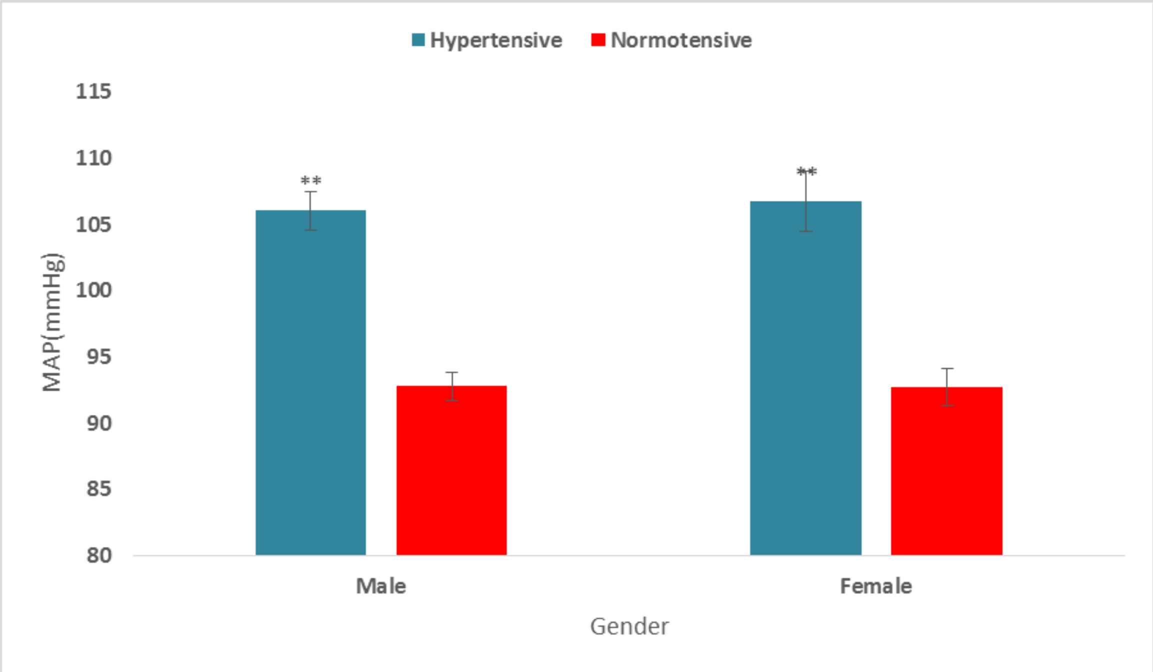

Figure III: Comparative Changes in Mean Arterial Pressure of Normotensive and Hypertensive Male and Female subject.
*** = significantly increased (at p < 0.05) compared to control (Normotensives)*

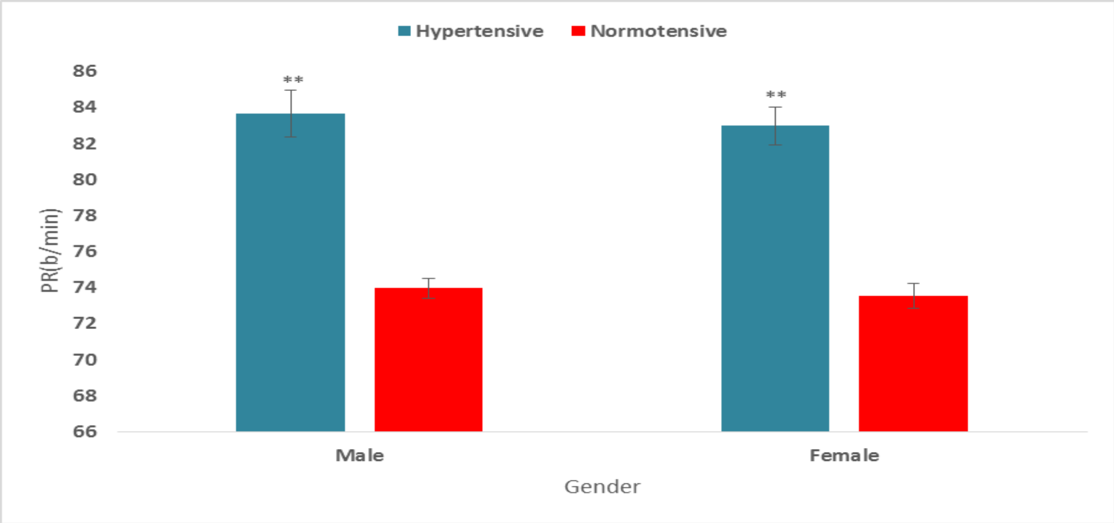

Figure IV: Comparative Changes in Pulse Rate of Normotensive and Hypertensive Male and Female subject
*** = significantly increased (at p < 0.05) compared to control (Normotensives)*

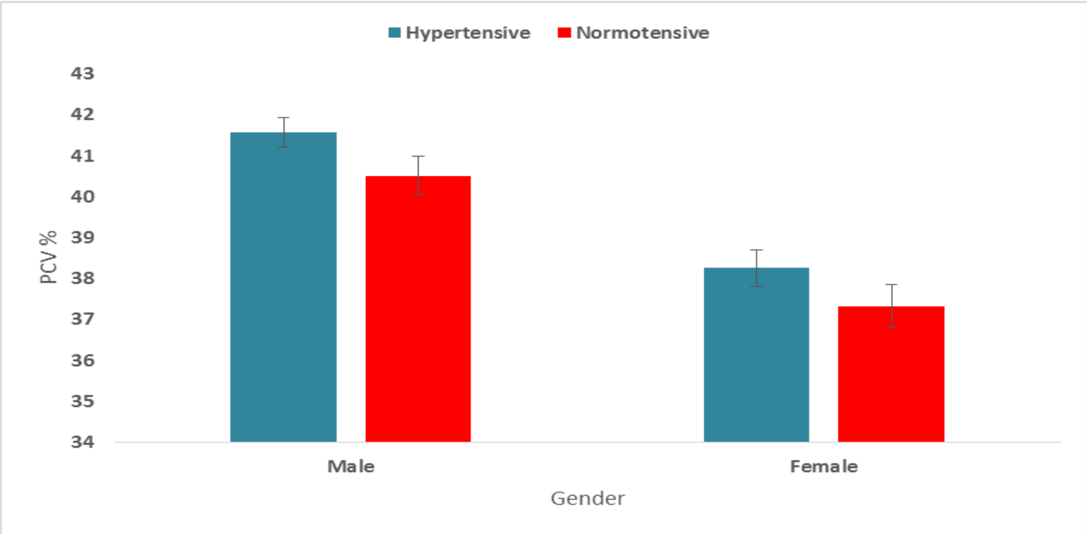

Figure V: Percentage Changes in PCV of Normotensive and Hypertensive Male and Female subjects.

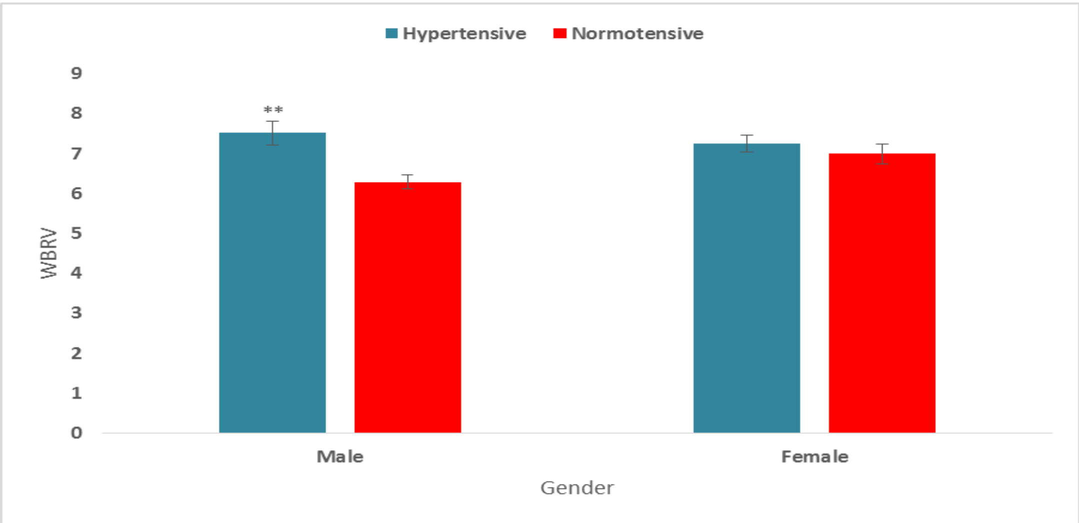

Figure VI: Percentage Changes in Whole Blood Viscosity of Normotensive and Hypertensive Male and Female subjects.
*** = significantly increased (at p < 0.05) compared to control (Normotensives)*

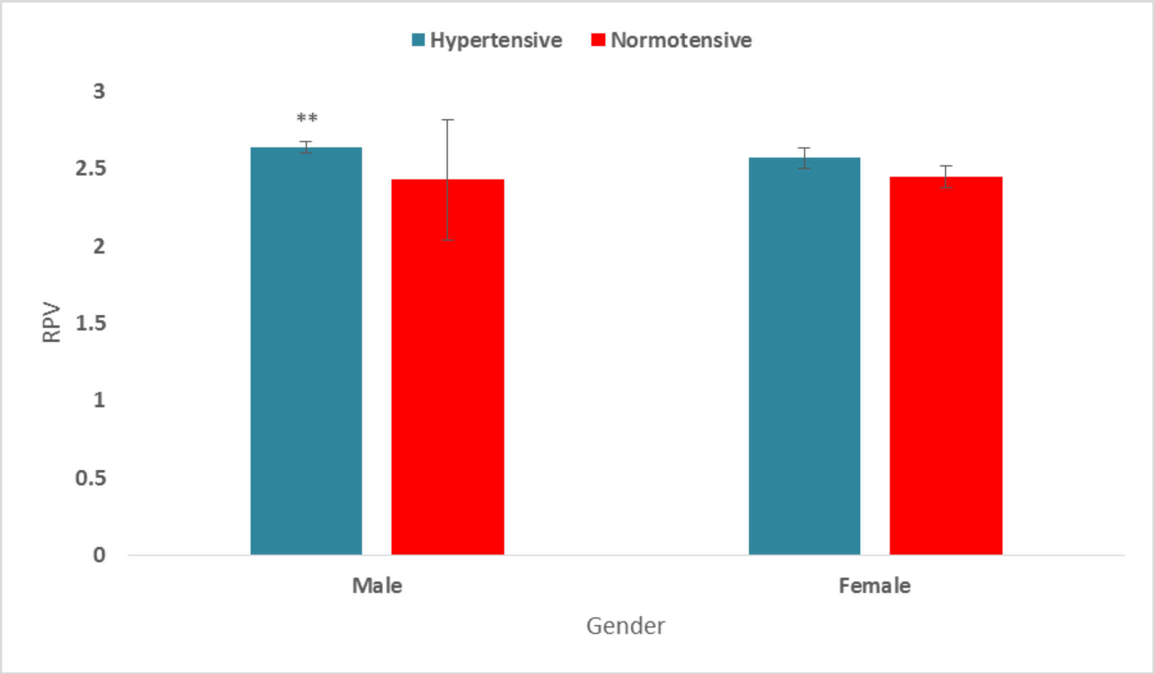

Figure VII: Percentage Changes in Relative Plasma Viscosity of Normotensive and Hypertensive Male and Female subjects.
*** = significantly increased (at p < 0.05) compared to control (Normotensives)*

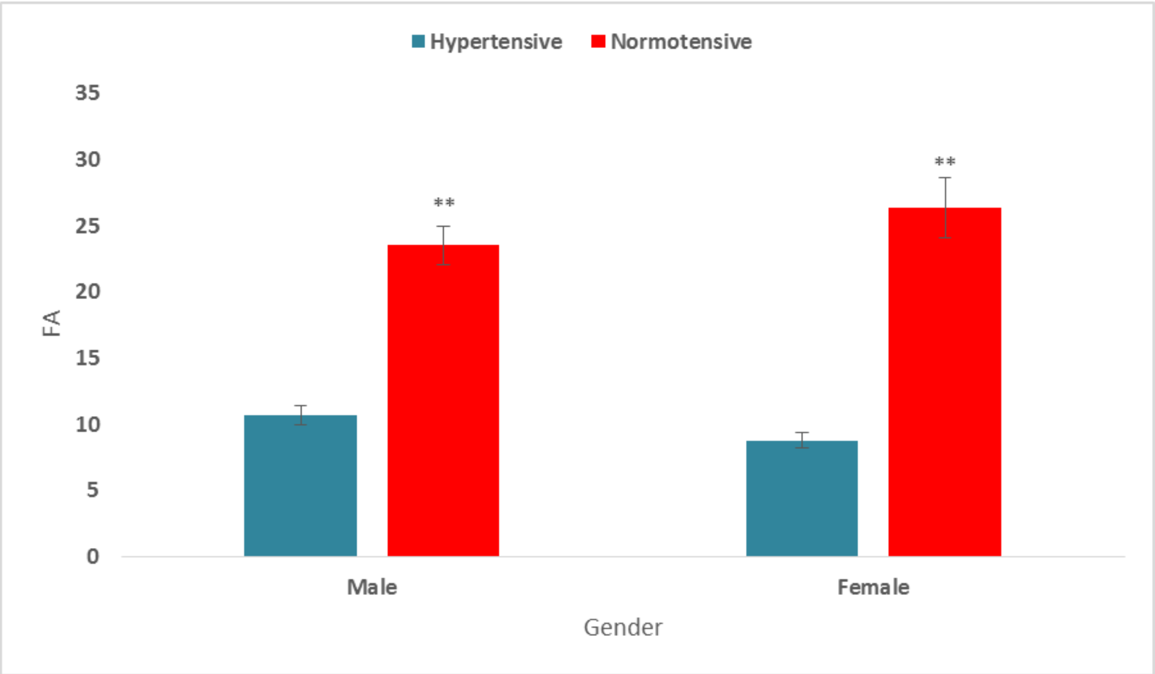

Figure VIII: Percentage Changes in Fibrinolytic Activity of Normotensive and Hypertensive Male and Female subjects.
*** = significantly increased (at p < 0.05) compared to control (Normotensives)*

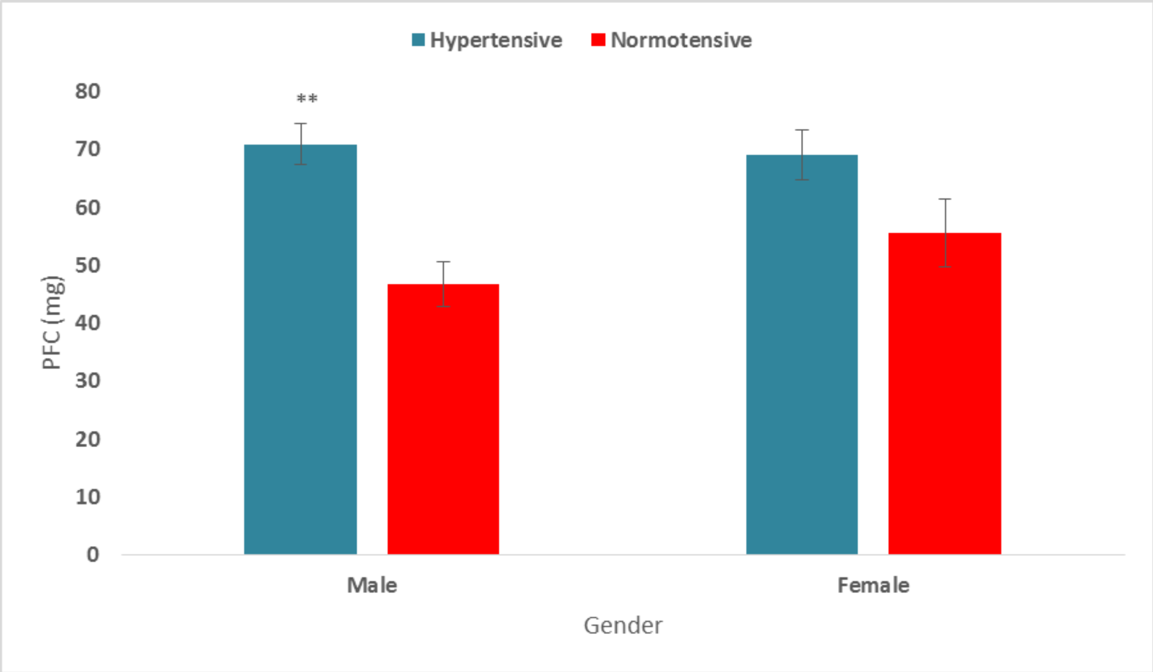

Figure IX: Percentage Changes in Plasma Fibrinogen Concentration of Normotensive and Hypertensive Male and Female subjects

DISCUSSION

This study aimed at comparing the hemorheological characteristics in hypertensive and normotensive subjects. The objectives were strictly adhered to. One hundred and forty subjects were used for this study, comprising of 70 normotensive and 70 hypertensive individuals.

Obtained data showed that the weight and BMI of hypertensives was significantly (p<0.01) higher than that of normotensives, various reports suggests that this could be a contributory factor to the development of elevated blood pressure. (Reisin *et al*, 1978). Also, mean systolic blood-pressure in the normotensive subjects; 120.67±1.09 mmHg and 142.89±1.61mmHg in the hypertensive reported, indicated that there is a significantly (p<0.01) higher systolic blood pressure in the hypertensive than the normotensive individuals. The same significant trend was observed in DBP and MAP of the hypertensive.[13] This supported a significant higher difference in blood pressure of hypertensive than the normotensive subjects.

Relative plasma viscosity(RPV) and plasma fibrinogen concentration(PFC) was observed to be significantly (p < 0.01) higher in hypertensives than in normotensives, packed cell volume (PCV) and Relative whole blood viscosity were also higher among hypertensives compared to normotensive but the increase was significant. Only fibrinolytic activity was observed to be significantly (p<0.01) higher in normotensives compared with their hypertensive counterpart.

As a major determinant of blood viscosity, Plasma viscosity noticeably caused an increase in the density of the plasma protein, plasma viscosity also increase but different proteins have different effects on the rate of plasma viscosity. Although there are high correlations between fibrinogen and plasma globulin with plasma viscosity, the increase of albumin level has less effect on the plasma viscosity.[14] Relative plasma viscosity is an important haemorheological parameter in hypertensive Nigerians.[15] Increased plasma viscosity in hypertensives may in turn result from higher fibrinogen levels[16] which may arise from a chronic-phase protein reaction, possibly associated with the increased catecholamine release in hypertension. Plasma viscosity is frequently elevated, due to alterations in the plasma protein content.[17]

In Caucasians several studies have reported that haemorheologic changes occur in hypertension. These studies have shown increases in plasma and whole blood viscosity.[18]

Whole blood relative viscosity was significantly higher in male hypertensives compared with male normotensives, similar result was also reported by Ighoroge and Dapper (2015). In hypertensive females whole blood relative viscosity was also higher than that of normotensive female but the increase was not significant. Whole blood relative viscosity was significantly higher in normotensive female than male normotensive the reason is not clear.

Hematocrit was higher in hypertensives but it was not significant but in contrast to Neuhaus *et al*, (1992) whose study observed that hematocrit shows big differences which make it hard to compare viscosity without considering the hematocrit rate. Male subjects in both hypertensive and normotensive groups had hematocrite values which was significantly higher than that of females In both groups, this is likely because the primary determinants of blood viscosity are highly affected by a woman's monthly blood loss. The effect on hematocrit is obvious: the monthly loss of 1 to 3 oz of blood will decrease the volume of RBCs. The effect on RBC deformability may be less obvious. Because of monthly bleeding, a woman makes more new blood cells than a man. Her blood contains about 80% more young blood cells and about 85% fewer old blood cells.[19]

Fibrinogen, a plasma protein, contributes more than other proteins to plasma viscosity in healthy subjects[15] This contribution is greatly increased in disease states[17], particularly in hypertension. In this study Plasma fibrinogen concentration was significantly (p<0.01) higher in hypertensives than normotensives in both male and female this was similar to the result gotten from various studies[20], but there was no significant different between age groups in both gender. The basis for increased fibrinogen concentration in patients with hypertension is not clear. But it is suggested that, plasma volume tends to be lower in hypertensive patients when compared to normotensive controls. This haemoconcentration may cause abnormally increased plasma fibrinogen.[21] It may be argued that the increase in plasma fibrinogen level was simply due to a response to stress as fibrinogen is known to be an acute phase reactant.[21]

Euglobulin clot lysis time is inversely proportional to fibrinolytic activity suggesting that in our study fibrinolytic activity is decreased. Euglobulin clot lysis time shows highly significant increase (decrease fibrinolysis) in hypertensives compared to normotensives. This suggests that as duration of hypertension increases, there are more chances of development of thrombotic complications.[20] A reduction in fibrinolytic activity may be in association with increased levels offibrinogen, plasminogen, and antiplasmin activity has been reported in patients with hypertension.[22 & 23]

CONCLUSION

Heamatocrit, relative plasma viscosity, whole blood relative viscosity and plasma fibrinogen concentration was significantly higher in hypertensive subjects, while fibrinolytic activity was significantly lower in hypertensive subjects. Thus, Haemorheological changes are associated with hypertensive state across all age groups.

REFERENCES

1. Nwosu, C. N., Nwabueze, A.C, and Ikeh, V. O. (1992): Stroke at the prime of life: a study of Nigerian Africans between the ages of 16 and 45years. *East Afr. Med. J,* 69(7): 384-390.
2. Palatini, P., Julius, S. and Julius (2009)."The role of cardiac autonomic function in hypertension and cardiovascular disease".*Curr.Hypertens. Rep,* 11(3): 199–205.
3. Perez-Martin, A., Dumortier, M., Pierrisnard, E., Raynaud, E., Mercier,J. and Brun, J.F.(2001).Multivariate analysis of relationships between insulin sensitivity and blood rheology: is plasma viscosity a marker of insulin resistance? *Clin.Hemorheol.Microcirc,* 25: 91–103.
4. Prisco, D., Paniccia, R., Bandinelli, B., et al. (1998). Evaluation of clotting and fibrinolytic activation after protracted exercise.*Thrombosis Research,* 89: 73-8.
5. Prokopowicz, J., Worowski, K., Poplawski, A., Gabryelewicz, A. and Niewiarowski, S. (1967). Fibrinolytic system in patients with hypertensive, cardiovascular disease. *Thrombos. Diathes. Haemorrh.*(Stuttg.), 17: 1-7.
6. Rand, P. W., Barker, N. and Lacombe, E. (1970).Effects of plasma viscosity and aggregation in whole blood viscosity.*Am. J.Physiol,* 218: 115-23.
7. Reid, H. L., Obi, G. O. And Oli, J. M.(1984). Reduced erythrocyte deformability and hyperfibrinogenemia in Nigerian diabetics with hemoglobin genotype HbAA. *Acta Diabetol. Lat,* 21: 105-14.
8. Reid, H .C and Ugwu, C .A (1987): A simple technique for rapid determination of plasma viscosity. *Nig. J. Physiol. Sci,* 3: 45-48.
9. Reisin E, Abel R, Modan M, Silverbag DS, Eliahou HE, Modan B. (1978) Effect of weight loss without salt restriction on the reduction of blood pressure in overweight hypertensive patients. *N. Engl. J. Med,* 298: 1-6.
10. Rodriguez-Cruz, E. and Ettinger, L. M. (2010)."Hypertension".eMedicinePediatrics: Cardiac Disease and Critical Care Medicine. Medscape. Retrieved 16 June 2009.
11. Ross, R. (1999). Atherosclerosis – an inflammatory disease. *N. Engl. J. Med.,* 340: 115-126.
12. Ingram, G. K. (1961). A suggested schedule for the rapid investigation of acute haemostatic failure. *J. Clin. Path,* 41: 521-534.
13. Schmid-Schonbein, H., Desai-Rohrig, L. (2002). Synergetics of blood flow in exercising skeletal muscle in man: cooperative effects of rheology, neurogenic vasoconstriction and mechanical effects of muscle pumps. *Biorheology,* 39.
14. Schmid-Schönbein, H., Foerster M., Heidtmann, H., Hektor J. et al. (2002). Percolation theory as the rational basis of clinical hemorheology: the role of "abnormal" flow behaviour of blood elements on the homogeneity of perfusion, gas exchange and metabolism, Biorheology, 39, (abstract).
15. Smutok, M.A, Recce C., Kokkinos, P.F., Farmer, C, and Goldberg, A.P. (1993). Aerobic versus stregnth training for risk factor intervention in middle-aged men at high risk for coronary heart disease. Metabolism, 42: 177-184.
16. Stoeff, S., Jovtchev, S. And Trifonova, N.(2012). Whole blood viscosity assessment in arterial

hypertension: a mathematical approach. *Series on Biomechanics*, 27: 30-33.
17. Sundström, Johan; Arima, Hisatomi; Jackson, Rod; Turnbull, Fiona; Rahimi, Kazem; Chalmers, John; Woodward, Mark; Neal, Bruce (2015). "Effects of Blood Pressure Reduction in Mild Hypertension". *Annals of Internal Medicine,* 162: 184–91.
18. Taj Muhammad Khan, Mumtaz Ali Marwat, Habibur Rehman, (2005).comparison of plasma viscosity and fibrinogen concentration in hypertensive and normotensive diabetics .*J Ayub Med Col Abbottabad*, 17(4).
19. Temiz, A., Baskurt, O.K., Pekcetin, C., Kandemir, F. and Gure A. (2000). Leukocyte activation, oxidant stress and red blood cell properties after acute, exhausting exercise in rats. *Clinical Hemorheology and Microcirculation*, 22: 253–259.
20. Vayá, A., Martínez, M., Garcia, J., Labios, M. and Aznar, J. (1992). Hemorheological alterations in mild essential hypertension. *Thromb Res,* 66(2-3): 223-9.
21. Wells, R. E., Denton, R. and Merrill, E. W. (1961).Measurement of viscosity of biologic fluids by Cone-Plate Viscosity of biologic fluids by Cone-Plate viscometer.*Journal of Laboratory and Clinical Medicine*, 57: 646-656.
22. West, J. B. (1990). Physiological basis of medical practice. 12th ed. Williams and wilkins, PPL, 139-144: 766-769.
23. Zannad, F., Voisin, P., Brunnote, F., Bruntz, J. F., Stoiz, J. F. andGilgenkrantz, J. M.(1988). Haemoreological abnormalities in arterial hypertension and their relation to cardiac hypertrophy.*J. Hypertension*, 6: 293-7.
24. Zinngg, W. and Shepley, D.J. (1970). Rheology and blood flow. *The Canadian Journal of Surgery*, 13: 177-182.