PROTHROMBIN TIME, ACTIVATED PARTIAL THROMBOPLASTIN TIME AND OTHER HAEMATOLOGICAL PARAMETERS AMONG NON-DIABETIC HYPERTENSIVE PATIENTS

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ABSTRACT
Objectives: To screen non-diabetic hypertensive Nigerian patients with a view to determining their haematological and coagulation profiles.

Subjects and Methods: Thirty (30) consecutive non-diabetic hypertensive patients, aged 20-60 years and 30 age and sex-matched, apparently healthy subjects, were investigated for some haematological and coagulation parameters, blood pressure, pulse, body weight, height and body mass index.

Results: There were statistically significant differences (p<0.05), in some haematological parameters, blood pressure, body mass index and height in the total number of patients studied when compared with the total control group. The separate genders each showed statistically significant differences in both haematological parameters and blood pressure (P<0.05) when compared with their corresponding control groups. In addition, haematological values, body mass index and height showed statistically significant differences (p<0.05) when the male and female patients were compared. Overall, 25 (83.33%) of the patient's blood films were normochromic and normocytic.

Conclusion: It appears that hypertension has adverse effects on haematological parameters. We therefore recommended that coagulations studies should be included in the investigation work-up of hypertensive patients.

INTRODUCTION

Cardiovascular disease is the main cause of death in the developed world[1], and there is growing evidence that a similar epidemic is inevitable for the developing world, if current trends continue unchecked[2]. Hypertension has for long been globally recognized as the most prevalent cardiovascular disease and is an acknowledged potent risk factor in the development of such disease outcomes as coronary heart disease, stroke, congestive heart failure and renal insufficiency. A direct positive relationship between blood pressure and cardiovascular risk has long been established[3]. This relationship is strong, continuous, graded, consistent, independent, predictive, and etiologically significant for those with and without coronary heart disease[4]; it has been identified in both males and females, younger and older adults, different racial and ethnic groups, different

countries; and applies to those within high-normal blood pressure as well as those with hypertension[5].
After adjusting for age and in line with the revised criteria by the World Health Organization (WHO, 1999)[6], an overall 16.6% or 7.8million of the 46.91million Nigerian population aged 15years and above were believed to be hypertensive. Patients with hypertension have a tendency to die prematurely; the most common cause of death being heart disease, stroke[7], and/or renal failure[8]. The health burden in Nigeria (the index country of study) resulting from hypertension is quite considerable[9].
Newly recognized risk factors that influence the development of cardiovascular disease include polymorphisms in the gene that encode fibrinogen and platelet glycoprotein II_b/III_a receptors. Specifically, a positive association exists between polymorphisms in the fibrinogen $B\beta448$ and platelet glycoprotein III_aP1^A genes and the extent of coronary artery disease[10]. Transient thrombosis and vasoconstriction cause unstable angina. Platelet-initiated thrombus increases local concentration of

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thromboxane A_2, serotonin, adenosine diphosphate (ADP), platelet activating factor, oxygen derived free radicals, tissue factors etc.

Furthermore, the risks associated with a given blood pressure are dependent upon the combination of risk factors[11]. However, the role and concentration of coagulation factors among non-diabetic hypertensive patients to the best of our knowledge is unknown and has been scarcely studied. Hence, this study was undertaken to screen non-diabetic hypertensive patients with a view to determining their haematological and coagulation profiles.

SUBJECTS AND METHODS

A. Place of Study
The study was done at the University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu, Nigeria a 700-bed hospital providing tertiary health care. The hospital is designated the National Cardiothoracic Centre of Excellence in Nigeria, and thus draws its patients population from all over Nigeria. Most of the patients, however, come from the adjoining 13 of the 36 states of the country.

B. Type of Study
(i) **Ethical Approval:** Clearance was obtained from the relevant authorities of the hospital.
(ii) The study group was drawn from consecutive hypertensive patients attending the medical out patients (MOP) and cardiac clinics of the University of Nigeria Teaching Hospital.
(iii) Inclusion Criteria: Adult patients within the young adult to middle age group (20 60 years) of both sexes; newly diagnosed to have hypertension and those who had not been on their antihypertensive treatment for at least two weeks prior to recruitment; who were willing to participate in the study, were included. They were enrolled with informed consent obtained, after explaining the objective of the study to them.
(iv) Exclusive Criteria: This included cases of diabetes mellitus, heart failure, valvular, congenital and ischaemic heart diseases, thyrotoxicosis, anaemia, acute febrile illness, stroke, liver diseases, pregnant and pueperal females (up to three months post partum), subjects on haemodialysis, antihypertensive drugs, steroids and oral contraceptives.

C. Sample Population
Patients referred to, and attending, the medical out patients and cardiac clinics of the University of Nigeria Teaching Hospital were screened for the study, between March to May, 2003.

The 30 consecutive patients, who met the Inclusion criteria, were enrolled for the study. They were divided into two equal groups of fifteen (15) males and females respectively. Two control groups of 15 males and 15 females were also studied. This brought the total number of subjects studied to sixty (60).

D. Study Design
History was taken from the patients, after which clinical examination was done, in order to establish the diagnosis of hypertension, by one of the authors, a cardiologist. Biodata and clinical parameters were recorded.

Routine chest radiograph, serum electrolytes, blood urea and creatinine, fasting blood glucose and urinalysis were carried out to rule out the exclusion criteria indices.

Necessary haematological tests were then done, employing standard manual methods with appropriate controls in all laboratory investigations.[12]

Controls: On enrolment of the non-diabetic hypertensive cases, suitable controls were identified. These were matched to the patients in age and sex and were not hypertensive. These control subjects included volunteering students, hospital staff and other patients undergoing a clinical check up and found to be healthy.

E. Measurements
(i) Physical age, sex, height, heart rate and blood pressure recordings were done.
(ii) Heamatological profile Haemoglobin (Hb), packed cell volume (PCV), Mean corpuscular haemoglobin concentration (MCHC), platelet count, erythrocyte sedimentation rate (ESR), Total and differential white blood cell count, such as neutrophils, lymphocytes, eosinophils, monocytes, and basophils, prothrombin time (PT) and Activated partial thromboplastin time (APTT).

F. Statistical Analysis
Data analysis was by computer, using EPI Info (version 6) statistical software.[13] Data Storage was in Microsoft Word XP 2000.[14]

Data are expressed as mean (standard deviation). P. values less than 0.05 were regarded as significant.

RESULTS
Figure 1 shows that there were 30 males and 30 females, with male, female ratio 1:1. The ages ranged from 20 to 60 years with mean 44.3. The 41 50 aged group recorded the highest number of subjects.

There were statistical differences ($p<0.05$) in Hb. PCV, platelet, ESR, total WBC, neutrophil, lymphocyte, and monocyte counts, PT, APTT, BP, height and BMI in the patients when compared with the control group (table 1).

There were also statistical differences (p<0.05) in Hb, PCV, ESR, lymphocyte, eosinophil, monocyte counts, PT and BP in the male patients when compared with the male controls (table 2).

Table 3 reveals statistical significant differences in Hb, ESR neutrphil, eosinophil counts, BP, height and BMI (p<0.05) in the female patients when compared to the corresponding females control.

The lymphocyte, monocyte counts, height and BMI indices showed statistically significant differences (p<0.05) when the male and female patients were compared (table 4).

Overall 25 (83.33%) of the non-diabetic hypertensive patients blood film showed normal (normochromic and normocytic) blood picture.
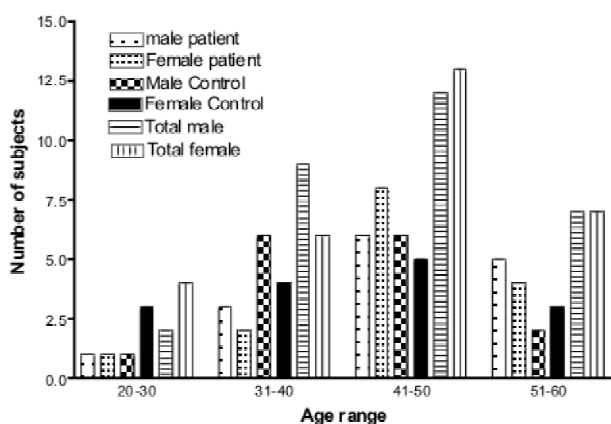
Figure 1: **Age and Sex Distribution of Subjects.**

Table 1: **Comparison between the Patients with the Control (Non-Diabetic Hypertensive) Group.**

Parameter	Patients	Controls
	N=30	N=30
	Mean (SD)	Mean (SD)
Prothrombin Time (S)	15.60 (3.67)	12.80 (1.28) *
Activated Partial Thromboplastin Time (S)	30.10 (4.66)	31.40 (3.32) **
Systolic (mm/Hg)	159.70 (19.07)	113.8 (8.55) ***
Diastolic (mm/Hg)	100.05 (10.42)	78.31 (5.31) ***
Pulse (b/min)	76.50 (8.83)	76.20 (3.24)
Weight (Kg)	75.20 (15.85)	69.60 (10.43) ***
Height (m)	1.66 (0.13)	1.73 (0.36)
Body Mass Index (Kg/m²)	27.99 (5.27)	23.42 (3.21) ***
Age (Years)	46.00 (12.23)	41.00 (8.91) ***
Haemoglobin (g/dl)	11.80 (2.19)	13.10 (1.32) ***
Packed Cell Volume (%)	34.50 (5.97)	39.30 (4.27) ***
Mean Corpuscular Haemoglobin Conc. (g/dl)	33.610 (1.31)	33.50 (0.71)
Platelet (X 10⁹/l)	189.30 (55.12)	242.20 (84.06) ***
Erythrocyte Sedimentation Rate (mm/hr)	18.92 (8.67)	7.9 (5.23) ***
Total White Blood Cell (X 10⁹/l)	6.00 (1.89)	6.80 (2.10) *
Neutrophil (%)	45.20 (16.93)	57.80 (11.54) ***
Lymphocyte (%)	52.10 (16.93)	39.70 (12.05) ***
Eosinophil (%)	1.60 (2.23)	1.80 (1.68)
Monocyte (%)	1.00 (1.74)	1.90 (2.02) *
Basophil (%)	0.00 (0.00)	0.00 (0.00)

P- Value when compared with the control group: * p

Table 2: **Comparison between the Male Patients with Male Controls.**

Parameters	Test	Control
	N = 15	N = 15
	Mean (SD)	Mean (SD)
Prothrombin Time (S)	16.53 (3.37)	13.07 (1.14)***
Activated Partial Thromboplastin Time (S)	29.27 (4.96)	31.03 (3.27)
Systolic (mmHg)	155.27 (13.97)	110 (11.33)***
Diastolic (mmHg)	98.6 (10.66)	80 (5.55)***
Pulse (b/min)	74.33 (7.51)	76.13 (3.97)
Weight (Kg)	73.73 (13.18)	68.87 (12.10)
Height (m)	174 (0.08)	1.74 (0.05)
Body Mass Index (Kg/m²)	24.59 (4.72)	22.54 (3.76)
Age (Years)	47.20 (10.54)	40.27 ()
Haemoglobin (g/dl)	12.13 (2.59)	13.53 (1.16)*
Packed Cell Volume (%)	34.73 (6.91)	40.67 (4.49)**
Mean Corpuscular Haemoglobin Concentration (g/dl)	33.73 (1.43)	33.43 (0.75)
Platelet (x 10⁹/L)	168.1 (155.36)	256.27 (116.97)
Erythrocyte Sedimentation Rate (mm/1ˢᵗhr)	15.14 (7.37)	9.87 (6.21)*
Total White Blood Cell (x 10⁹/L)	5.84 (2.17)	6.06 (2.15)
Neutrophil (%)	48.53 (19.79)	57.20 (13.60)
Lymphocyte (%)	42.27 (19.79)	42.53 (13.28)***
Eosinophil (%)	1.87 (1.82)	1.73 (1.46)*
Monocyte (%)	0.53 (0.82)	1.70 (1.60) ***
Basophil (%)	0.00 (0.00)	0.00 (0.00)

P-Value when compared with control group * P < 0.01, ** P < 0.001, *** P < 0.0001

Table 3: **Comparison between the Female Patients with Female Control**

Parameters	Test	Control
	N = 15	N = 15
	Mean (SD)	Mean (SD)
Prothrombin Time (s)	14.60 (2.26)	13.33 (2.78)
Activated Partial Thromboplastin Time (s)	30.9 (4.75)	31.84 (3.47)
Systolic (mmHg)	164.13 (26.93)	117.67 (7.30)***
Diastolic (mmHg)	102.33 (9.76)	76.67 (4.79)***
Pulse (b/min)	78.67 (10.80)	76.27 (12.26)
Weight (kg)	76.67 (21.43)	70.33 (9.20)
Height (m)	159 (0.14)	1.71 (0.11)***
Body Mass Index (kg/m²)	31.40 (8.12)	24.3 (4.81)*
Age (year)	45.3 (9.34)	41.6 (10.73)
Haemoglobin (g/dl)	11.55 (1.87)	12.71 (1.17)*
Packed Cell Volume (%)	34.27 (5.09)	37.93 (3.65)
Mean Corpuscular Haemoglobin Concentration (g/dl)	33.47 (1.38)	12.71 (0.61)
Platelet (x 10⁹/L)	210.47 (62.52)	228.13 (70.12)
Erythrocyte Sedimentation Rate (mm/1ˢᵗ hr)	12 (8.37)	6 (4.17)*
Total White Blood Cell (x 10⁹/L)	6.2 (1.62)	6.91 (2.081)
Neutrophil (%)	38.93 (13.02)	58.47 (8.86)***
Lymphocyte (%)	58.40 (11.21)	36.87 (10.12)
Eosinophil (%)	1.20 (1.97)	1.93 (1.36)*
Monocyte (%)	1.50 (1.80)	2.07 (1.72)
Basophil (%)	0.00 (0.00)	0.00 (0.00)

P-value * = P<0.01, ** = P< 0.001, *** = P< 0.0001

Table 4: **Comparison between the Male and Female Patients Group.**

Parameters	Male Test N = 15 Mean (SD)	Female Test N = 15 Mean (SD)
Prothrombin Time (s)	16.56 (3.37)	14.60 (2.26)
Activated Partial Thromboplastin Time (s)	29.27 (4.96)	30.9 (4.75)
Systolic (mmHg)	155.27 (13.97)	164.13 (7.30)
Diastolic (mmHg)	98.6 (10.66)	9.76 (4.79)
Pulse (b/min)	14.33 (7.51)	78.67 (10.80)
Weight (kg)	73.73 (13.18)	76.67 (21.43)
Height (m)	1.74 (0.08)	1.59 (0.14)***
Body Mass Index (kg/m²)	24.59 (4.72)	31.40 (8.12)**
Age (year)	47.20 (10.54)	45.30 (9.84)
Haemoglobin (g/dl)	12.13 (2.59)	12.71 (1.17)
Packed Cell Volume (%)	34.73 (6.91	37.93 (3.65)
Mean Corpuscular Haemoglobin Concentration (g/dl)	33.73 (1.43)	32.71 (0.61)
Platelets (x 10⁹/L)	168.1 (155.36)	228.13 (70.12)
Erythrocyte Sedimentation Rate (mm/hr)	15.14 (7.37)	6.00 (4.17)
Total White Blood Cell (x 10⁹/L)	5.84 (2.17)	6.91 (2.08)
Neutrophil (%)	46.53 (18.20)	38.93 (13.07)
Lymphocyte (%)	42.27 (19.79)	58.40 (11.21)**
Eosinophil (%)	1.87 (1.82)	1.20 (1.97)
Monocyte (%)	0.53 (0.83)	1.50 (1.80)
Basophil (%)	0.00 (0.00)	0.00 (0.00)

P-value * = P<0.01, ** = P< 0.001, *** = P< 0.0001.

DISCUSSION

Studies in the United States in community surveys over a period of 20 years, from 1971-72 and from 1988-91, showed an increase among hypertensive patients of awareness of their condition from 51-84%, and those on treatment from 36-73%. In contrast, only about a third of Nigerians who are hypertensive are aware of their condition, and about 2/3 of those who are aware are on treatment[15].

Among the haematological parameters studied, prothrombin time, activated partial thromboplastin time, haemoglobin, packed cell volume, platelet, erythrocyte sedimentation rate, total white blood cell count, neutrophil, lymphocyte and monocyte values showed statistically significant differences (p<0.05) in the patients when compared with the control group (table I). This is in line with results of similar studies[16] that established significant differences among hypertensive patients, although the prothrombin time and activated partial thromboplastin time were not studied in these works. The values obtained in the present work however, places hypertensive patients as being among the high-risk group for the detection of coagulation disorders. This may therefore bear out the need to routinely screen non-diabetic hypertensive patients for coagulation parameters/profile.

The blood pressure, height and body mass index showed statistically significant differences (p<0.05), between patients and controls (table 1). This observation is in keeping with the results obtained in hypertensive Nigerians by Akinkugbe et al,[15] who reported a strong correlation between the body mass index and the prevalence of hypertension.

This study has revealed statistically significant differences in prothrombin time, haemoglobin, packed cell volume, erythrocyte sedimentation rate, lymphocyte, eosinophil, monocyte counts and blood pressure measurements (p<0.05) when male patients were compared with apparently healthy male controls (table 2); however, there was no significant differences in other parameters studied. Furthermore, the haemoglobin, erythrocyte sedimentation rate, neutrophil, monocyte, height and body mass index showed statistically significant differences (p<0.05) when the female patients were compared with the female controls (table 3). Although the differences in prevalence of hypertension among medical admissions in both sexes (males, 15.4% and females 14.9%) in Eastern Nigeria in a work done at the same study location, was not significant[9], the present study revealed that male non-diabetic hypertensive patients are more predisposed to coagulation defects than their corresponding female patients (tables 2 and 3). This may be attributed to more exerting physical activities, alcohol consumption, cigarette smoking and lower level of awareness among male hypertensive patients as compared to the female hypertensive patients[6].

Also, lymphocytes, monocyte counts, and body mass index (BMI) demonstrated statistically significant differences (p<0.05) between the male and female patients, with higher levels in the latter. This may be attributable to the significantly higher BMI values in females as compared to the males of the same age. This observation lends itself to further larger population based study.

Generally, 25 (83.33%) of the non-diabetic hypertensive patients blood films revealed normal (normochromic and normocytic) blood picture.

CONCLUSION

This study has shown that hypertensive patients present with abnormal prothrombim time, activated partial thromboplastin time and other haematological parameters. It is, therefore, being recommended that, regular routine coagulation studies should be carried out on hypertensive patients, as part of their clinical investigation.

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