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HAEMOSTATIC FACTORS ASSESSMENT AMONG MALE AND FEMALE GERIATRICS IN NNEWI, ANAMBRA STATE NIGERIA.

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ABSTRACT

Background: Coagulation profiles are very important assay carried out in the assessment of Haemostatic factors. The coagulation factors are present in the blood and helps in regulating the loss of blood through injury, internal bleeding, during surgery, monitoring oral anticoagulant therapy and evaluating the function of the liver. The absent or reduction of these coagulation factors lead to excessive bleeding which may lead to death. Some of these coagulation profiles are Platelet count, Prothrombin Time (PT), Activated Partial Thrombin Time (aPTT), Whole blood Clothing Time (CT) and Bleeding Time (BT) and were carried out among 100 male and 100 female geriatrics residing in Nnewi, Anambra state, Nigeria. Their ages ranges from 65 years to 84 years old. Young adult aged 18-25 years blood samples were used as control. The results showed the geriatrics values higher than the control samples. The PT of female geriatrics significantly ($p = 0.03$), higher than the male geriatrics, while the aPTT of male geriatrics significantly ($p = 0.00$) higher than the female geriatrics. The platelets values, INR, the clotting and the bleeding time levels did not differ between the male and female geriatrics. With these result, the male and female geriatrics health can be assessed and treated adequately.

KEYWORDS: Haemostatic's factors, male geriatrics, female geriatrics, Nnewi.

INTRODUCTION

Ageing is a general physiology process which affects cell and the systems made up of them, as well as tissue components.[1] In old age red bone marrow sites are slowly replaced with yellow inactive marrow.[1] Red marrow forms all types of blood cells and it is also one of the largest and most active organs of the human body,[1] and prolonged Clotting time has been observed in the aged due to decline in platelets count, coagulation factors and serum calcium concentration.[2]

Haemostasis as a word is taken from the Greek word, Haem meaning blood and stasis meaning standing. It is a process which causes bleeding to stop thereby stopping blood from escaping through damaged blood vessel.[3] Haemostasis is very important because it arrests bleeding (clot formation) when blood vessels are damaged which if the bleeding is not arrested (sudden and severe loss of blood) can lead to shock and death.[4] Haemostasis changes with aging as a result of change in coagulation factors, thrombin generation, and platelet function. Platelet activation and most coagulation factors (fibrinogen, factor V, VII, VIII, IX, XI, XIII, and VWF) increase with age.[2] Several studies have shown that this translates into increased thrombin generation.[5] At the same time, fibrinolytic activity slows with age.[6] Besides these dynamics, aging is associated with change in endothelium, blood flow through the vasculature and impaired renal function, all affecting how haemostatic agents interact and ultimately influencing coagulation. During haemostasis three steps occur in a rapid sequence. Vascular spasm is the first response as the blood vessels constricts to allow less blood to be lost.[7] In the second step, there is platelets plug formation, platelet stick together to form a temporary seal to cover the break in the vessel wall.[8] The third and last step is called coagulation or blood clotting Blood coagulation-Clots form upon the conversion of fibrinogen to fibrin, and its addition to the platelet plug (secondary

haemostasis). Coagulation uses fibrin threads that act as a glue for the sticky platelets. As the fibrin mesh begins to form the blood is also transformed from a liquid to a gel like substance through involvement of clotting factors and pro-coagulates.[9]

Haemostasis can produce significant discrepancies between normal ranges of coagulation studies, such as the Prothrombin time and activated partial thromboplastin time (aPTT), depending on age and prematurity.[3] With advancing age, many individuals who are otherwise normal show laboratory evidence of increase of coagulation enzyme activity. PT, INR and aPTT levels shows slight differences in certain age and gender,[10] Prothrombotic clotting factor; the plasma concentration of several clotting factors namely fibrinogen factor vii, factor viii, Von willebrand factor (VWF) factor ix, factor xii increase with progressing age in healthy individuals.[11]

Prothrombin time (PT) assay is a test extensively used in extrinsic coagulation pathway evaluation.[12] PT is used for diagnosing coagulation disorders, evaluating liver functions and determining the risk of bleeding prior to surgical intervention. It is the most commonly used coagulation test in routine laboratories.

International normalized ratio (INR), which was introduced to overcome the problem of marked variation in PT results among laboratories, has been used to standardize PT value. The INR level is used to measure the extrinsic pathway of the coagulation cascade and influenced by coagulation factors I (fibrinogen), II (prothrombin), V, VII, and X. Different methods have been used for monitoring of anticoagulant therapy, however, the standard reporting method used in many countries is the INR.[12]

Activated partial thromboplastin time (aPTT) is a screening test for deficiency of factors II, V, VIII, IX, X, XI and XII of the intrinsic and common pathways.[12]

Clotting time is determined by the quantum of platelets in the blood, is dependent on coagulation. Blood coagulation involves a biological amplification system in which relatively few initiation substances sequentially activate by proteolysis a cascade of circulating precursor proteins (the coagulation factor enzyme) which culminates in the generation of thrombin; this, in turn, converts soluble plasma fibrinogen into fibrin,[13] Hence a decrease platelet counts can prolong clotting time and increased platelet counts can decrease clotting time.[13]

The first test for evaluation of platelet function is bleeding time (BT) test,[14] It is still one of the most important tests to assess platelet function and primary homeostasis,[15] BT is the period of time required to stop hemorrhage after an incision. While normal BT usually varies between 2-10 minutes (in some studies 2-9 minutes), it may increase to more than 30 minutes in severe platelet deficiency.[14;16] Gender is one of the factors that affect BT and greater values are observed in females.[14] Other factors such as skin temperature, exercise, anxiety, incisions longer than the standard incision, and excessive cleaning of the test area, affects BT.[17] Age was also found to alter BT.[18] Other researchers,[14;16] have shown that BT decreases by increasing age, different races and different areas throughout the world. It is hence necessary to determine normal BT in each geographical zone. Other factors which may prolong BT include white blood cell (WBC) and red blood cell (RBC) count, chronic kidney disease, anemia, connective tissue disorders (such as Ehlers-Danlos syndrome). Furthermore, some kinds of foods, vitamins and spices like ginger, curcuma, onion, vitamins E and C, and garlic, produce abnormal platelet aggregation and BT.[13] Coagulation and fibrinolytic activities are under strong genetic control.[19] Genetic factors contribute to individual variation of blood coagulation protein levels.[20] When the genes controlling the production of coagulation factors are mutated, abnormal results are obtained. Prothrombin time (PT) and activated partial thromboplastin time (APTT) has been shown to be associated with elevated systolic and diastolic blood pressures in hypertensive and normotensive patients.[21] Hypertension is a chronic medical condition in which the blood pressure is indisputably elevated (≥140/90 mmHg). It is one of the most common worldwide diseases afflicting humans and more especially the geriatrics.[22] Due to several associated morbidity, mortality, and economic cost to society, hypertension is now a serious public health challenge to both developed and developing nations.[23] and the health care providers have been advised to treat all injuries in the geriatrics as an emergency, since the geriatrics often expose themselves to injuries and cut. Despite considerable amount of data published concerning the coagulation status of the geriatrics, clinicians are still confronted with the problem of ‘‘Normal’’ or ‘‘physiological’’ values in these subjects. Hence the need to assess some of the coagulation profile among the male and female geriatrics residing in Nnewi, Anambra Nigeria.

MATERIAL AND METHOD

Three hundred subjects, 100 males, 100 females’ geriatrics age range 65-84years old and 100 young adults aged 18 – 25years (as control) all residing in Nnewi were used for the study. Six milliliter (6ml) ml of venous blood was collected with a 10ml syringe and 21G needle, 2.25 ml of the blood was dispensed into 0.25ml of sodium citrate in a sample bottle (9 parts of blood and 1 part of trisodium citrate) for prothrombin test (time and INR) and activated partial prothrombin test (time). This was mixed immediately and centrifuged for 1500g to obtain a plasma poor in platelet. The tests were carried out using CA-1500 (Sysmex, Kobe, Japan), with appropriate quality control materials and standard reagents (Dade Behring, Germany). Three milliliters were used for clotting time (Lee and white method),[1] 1

ml of blood was added in 3 different plain tubes fixed in a rack previously placed in a water bath at a temperature of 37ºC, each bottle was tilted to check for the sign of blood clot every 30 sec. using a stop watch, the time interval between blood collection and the time the clot appeared in each test tube was recorded in minutes. The average of the three reading was taken as the clothing time for each subject. The remaining blood in the syringes was added in Ethylene diamine tetra acetic tube (EDTA) for platelet count, which was carried out using sysmex automated heamatology analyser KY2IN model manufactured by Sysmex Corporation Kobe Japan. The bleeding time (BT) was performed by Ivy's modified template method,[1] sphygmomanometer cuff was wrapped around the upper arm and inflated to a pressure of 40mms of mercury and maintained throughout the test. The forearm was cleansed with alcohol pad and allowed to dry skin punctures were made on the anterior side avoiding superficial vein. The stop watch was started immediately the first puncture was made. The blood from the wound was then removed at regular intervals (15-30secs) using the edge of a filter paper, making sure not to touch the wound. The time taken for each bleed from to stop was noted separately and the average time taken,[24] All data was statistically evaluated by using SPSS version 21.0 (statistical package for social sciences). Values were expressed as mean ± standard deviation. The results were analyzed for statistical significance using the independent student T-test, P-value ≤ 0.05 were considered statistically significant.

RESULT

The table below showed the values of the young adult and the geriatrics. It revealed significant differences (P=0.03) in the mean ± SD of PT (secs.) result values among the male and female geriatrics. The female geriatrics had a PT value of 16.23 ± 2.0, higher than the male geriatrics with PT value of 15.04 ± 2.0. The mean ± SD of APT value for the male geriatrics showed 30.83 ± 6.34 and were higher than the mean values for female geriatrics (28.72 ± 5.34). There were significant differences (p=0.00) in APT values of male and female geriatrics. Platelet values, PT- INR values, clotting and bleeding time values, showed no significant differences in their mean values of the male and female geriatrics as shown on the table below.

Table: Coagulation Profile (Platelet, Pt, Inr, Aptt, Clotting And Bleeding Time) Values Among Male And Female Geriatrics Residing In Nnewi And Environs.

Hatolaemogical Parameters	Male Geriatrics (n=100)	Female Geriatrics (n=100)	P-Value	Adult Control (n=100)
Platelet Count($x10^9$/L)	188.23 ± 24.21	189.59± 29.22	0.59	206.45±2.44
PT (secs)	15.04 ± 2.0	16.23 ± 2.0	0.03*	13.87±0.07
PT-INR	1.19 ± 0.29	1.16± 0.14	0.09	1.06±0.07
APTT(secs)	30.83±6.34	28.72±5.34	0.00*	25.82±0.80
Clotting Time (mins)	4.50 ± 0.5	4.64 ± 1.6	0.20	4.42±0.63
Bleeding Time (mins)	1.47 ± 0 .3	1.58 ± 0 .6	0.37	1.47±0.29

Data is expressed as mean ± SD; * significant ($P \leq 0.05$)

DISCUSSION

In this study to assessment of some Haemostatic factors among male and female geriatrics in Nnewi, Anambra state Nigeria, we observed that the male and the female geriatric values were higher than the young adults values used as control, which is in line with a study.[25] on the effect of age on Prothrombin time (PT) activated partial thromboplastin time (APTT) on male and female above 60 years. Their result showed that elderly male and female values were significantly higher than the mean of the young control groups. We also observed significant differences ($p \leq 0.05$) among male and female geriatrics in their prothrombin time and activated partial thrombin time. The Platelet values, International normalized ratio, the whole blood clothing time and the bleeding time did not show any significant variation in their values ($p>0.05$). The increase of both PT and aPTT in the geriatrics suggests decrease of the common pathway coagulation factor (factor X, V, and II) or a qualitative or quantitative fibrinogen defect as age progresses, indicating the prothrombin time and activated partial thromboplastin time increases with age.[25] This observation may be as a result of the decrease of the red marrow by fatty tissue (yellow marrow).[1] increasing replacement of red marrow by fatty tissue with increasing age has been reported.[1] However, apart from replacement of the red marrow with fatty marrow being the reason for difference, this study confirmed that there is significant difference in some coagulation parameters between the males and the female's geriatrics as has been observed. This fact that the female individuals having comparatively increased prothrombin time can be due to the presence of estrogens, which decrease the level of fibrinogen in the plasma and increase the clotting time.[26] and also the occurrence of menopause in elderly women which is accompanied by a significant increase in antithrombin III plasma level coagulation system.[27] The male geriatrics had higher value of activated partial thrombin time than the female geriatrics, but other authors.[10] *in their study, reported that aPTT* levels did not differ between genders. The significant changes in activated partial thromboplastin time is attributed to the decrease of one or more of the intrinsic pathway clotting factors (prekallikrein, high molecular weight kininogen,

factor XII, XI, IX, and VIII.[27] The difference in gender among clotting time showed that females had clotting time value higher than the males but not statistically significant.

In this study we also observed statistical differences in the values of platelet counts of the geriatrics when compared with the adult control values.The pronounced decrease in the platelet counts in the geriatrics may be due to a decreased sensitivity to the specific inhibitor rotenone which affects the level of platelet counts.[28] The effect of aging on platelet may be related to reduce hematopoietic stem cell reverse in aging individuals.[29] The decrease in platelet during aging is also attributed to age dependent decline in platelet number which effect epigenetic changes in the megakaryocyte genome.[30]

CONCLUSION

In conclusion, the geriatrics had increased prothrombin time (PT) and activated partial thromboplastin (aPTT) while the platelet counts show a significant decrease when compared with the adult controls used. And from the study, we then suggest that the geriatrics should be considered when carrying out any investigations as to provide them with the necessary standard which can be used to accessed their health status.

CONFLICT OF INTEREST

There is no conflict of interest and no fund received for the study.

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