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ORIGINAL ARTICLE

Selected Indicators of Immunothrombosis in Apparently Healthy Nigerian Women of Different Reproductive Status

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Abstract

Women are considered to be vulnerable with regards to immunothrombotic conditions. Exploring this bidirectional susceptibility across the different female reproductive phases is important for effective maternal healthcare delivery. This study assessed selected indicators of immunothrombosis between premenopausal and postmenopausal women.

Methods: Equal numbers of premenopausal and postmenopausal women totaling one hundred were recruited for this comparative study. Blood sample was collected from each participant into appropriate sample bottles. Blood cell counts were carried out by haemocytometry and microscopic blood film reading. Standard manual methods were also employed for prothrombin time, activated partial thromboplastin time and relative plasma viscosity tests, while blood cell ratios were calculated. Results are expressed as Mean ±SD following student t-test analysis of data on SPSS version 22.0. Statistical significance was drawn at a $p \leq 0.05$.

Results: The eosinophils count ($0.42\pm0.31x10^9/l$), monocyte count ($0.05\pm0.05x10^9/l$) and platelets count ($150.04\pm46.88x10^9/l$) were significantly higher in premenopausal women than postmenopausal women ($0.29\pm0.27x10^9/l$, $0.03\pm0.03x10^9/l$ and $132.62\pm38.37x10^9/l$ respectively), while a significantly higher value was observed in the relative plasma viscosity of postmenopausal women (1.74±0.17mPa/s) than the premenopausal women (1.59±0.10mPa/s). The two derived indicators of inflammation (NLR) and thrombosis (PLR) correlated positively in both premenopausal ($r=0.397$, $p=0.004$) and postmenopausal ($r=0.293$, $p=0.039$) women.

Conclusion: Immune and thrombotic parameters are largely comparable in apparently healthy adult females irrespective of their reproductive phase. However, eosinophil, monocyte and platelet counts

were observed to be significantly higher in premenopausal women compared to postmenopausal women.

Key words: Immunity, thrombosis, immunothrombosis, menopause

Introduction

Inflammation and coagulation disturbance often arise from responses that are aimed at addressing specific triggers, yet their aetiology could also be pathological in nature. Whichever way, it is presently recognized that innate immunity and coagulation activation interrelate and contribute to the pathophysiology of various disease conditions (1,2). Apart from investigating disease conditions where inflammation and haemostatic dysfunction may be suspected, apparently healthy populations also deserve attention in this regard particularly with groups that are thought to be vulnerable (3-5). Basic screening of cellular response to inflammation and coagulation can be achieved through the leukocyte and thrombocyte parameters of the full blood count, while further investigation of coagulation status may be appreciated by assessing the intrinsic and extrinsic pathways of the coagulation cascade (6,7). In recent times though, blood cell counts have been further explored by deriving ratios within the differential white cell counts as well as between white cell sub-population and the platelets. Ranging from overall survival in relation to malignancies, the application of blood cell count derivatives extends to cardiovascular conditions, infections, degenerative disorders and risk categorization for vulnerable groups (8-11). Thus, these derivatives are currently recognized for their diagnostic and prognostic utilities in clinical practice (12-15).

As earlier observed, the crosstalk between inflammation and thrombosis appears to be more obvious in disease conditions than in physiological states (3,6,16,17). Howbeit, the female reproductive physiology recognizes inflammatory and coagulation changes modulated by the female reproductive hormones. Evident in the surge of white blood cells alongside a decline in the platelet counts close to the period of menstrual flow, the female body responds commensurately to the stress of the menstrual cycle (18-20). The general impact of this monthly response and attendant changes may not be fully known but could contribute to the greater predisposition of females to immunothrombotic mechanisms that underlie several disease conditions. Exploring this female-associated vulnerability across the different reproductive phases is important in other to decipher the direction of change that menopause exerts. While hormonal fluctuations characterize the premenopausal phase, postmenopausal women are faced with age-associated health complications. It is therefore important that indices of immuno-thrombosis are assessed between premenopausal and postmenopausal women for better understanding of maternal health.

Methods

Equal numbers of premenopausal and postmenopausal women totaling one hundred were recruited for this comparative study. These consenting study participants were apparently healthy and not on medication/ anticoagulant therapy within the preceding one year to the study period. Ethical considerations including confidentiality were maintained. A structured questionnaire was administered to obtain biodata as well as pertinent information with regards to participants' reproductive state and medical history.

Blood sample was appropriately obtained from each subject into dipotassium ethylene diamine tetra-acetic acid bottle at a concentration of 2mg/ml of blood for assessment of platelet count, total white blood cell count and differential white blood cell count. Additional volume of blood was dispensed into 3.13% trisodium citrate bottle at a ratio of 9:1. Haemocytometry and microscopic blood film reading were employed for blood cell counts. Quick's one-stage method was used for prothrombin time assay and modified kaolin method for activated partial thromboplastin time measurement. Relative plasma viscosity was assessed using a capillary viscometer. Blood cell ratios were mathematically derived. Data generated were entered into Microsoft excel spreadsheet and analysed using Statistical Package for Social Sciences (SPSS) software version 22.0. Results are expressed as Frequencies and Mean±SD, while Student t-test was used for comparison. Statistical significance was drawn at a $p \leq 0.05$.

Results

In this study, total white blood cell count (TWBC), differential white blood cell count (Neutrophils, Lymphocytes, eosinophils, monocytes and basophils) and Platelet count were assessed in premenopausal and postmenopausal women. From these parameters, blood cell count derivatives including neutrophil-to-lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were calculated across the groups. In addition, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT) and relative plasma viscosity (RPV) were also assessed in premenopausal and postmenopausal women.

The eosinophils count ($0.42\pm0.31x10^9/l$), monocyte count ($0.05\pm0.05x10^9/l$) and platelets count ($150.04\pm46.88x10^9/l$) were significantly higher in premenopausal women than postmenopausal women ($0.29\pm0.27x10^9/l$, $0.03\pm0.03x10^9/l$ and $132.62\pm38.37x10^9/l$ respectively), while a significantly higher value was observed in the relative plasma viscosity of postmenopausal women (1.74 ± 0.17mPa/s) than the premenopausal women (1.59 ± 0.10mPa/s) (Table 1). The two derived indicators of inflammation (NLR) and thrombosis (PLR) correlated positively in both premenopausal ($r=0.397$, $p=0.004$) and postmenopausal ($r=0.293$, $p=0.039$) women as shown in Figures 1 and 2 respectively.

Discussion

The present study compared total and differential white blood cell counts between premenopausal and postmenopausal women. Apart from eosinophil and monocyte counts which were observed to be significantly higher in premenopausal women than postmenopausal women, the other white blood cell parameters were comparatively similar irrespective of reproductive phase in these apparently healthy women. While reported views regarding actual direction of the influence of female reproductive hormones on the various white blood cell sub-populations remain divergent, it is consensually appreciated that the processes associated with immune response are more pronounced in females compared to males (21-23). The weight of evidence in support of this gender dimorphism is largely drawn from high female preponderance in relation to autoimmune disorders. Exploring the role of female reproductive hormones with regards to immune response and coagulation activation remains important for better understanding and management of immunothrombotic conditions, thus it represents an interest for future research.

The expression of significantly higher cellular response in peripheral blood of premenopausal women also extended to the platelet count. The events of the menstrual cycle culminate into the shedding of the uterine wall and

subsequent bleeding. It is, by nature, necessary that mechanisms for controlled bleeding exist as part of the adult female physiology. Higher platelet counts in premenopausal women have also been previously reported (24). Apparently, this precautionary plug becomes overtaken at the postmenopausal phase of womanhood as reproductive hormonal fluctuations cease and the level of the hormones generally decline. Another observed change at this stage is the increased relative plasma viscosity, which although is associated with advanced age, has also been reported to be significantly associated with other postmenopausal changes other than age (25).

Blood cell count derivatives have emerged as more sensitive prognostic markers than the traditional direct count themselves. In the present study, the two derived indicators of inflammation (NLR) and thrombosis (PLR) were comparatively similar in both groups. Moreso, these indicators correlated positively in both premenopausal and postmenopausal women, thus underscoring the interplay between immunity and haemostasis.

Table 1 The total blood white cell count, Differential white blood cell counts, Platelets count (PLT), blood cell count ratios, Prothrombin time, International normalized ratio, Activated partial thromboplastin time and Relative plasma viscosity of premenopausal and postmenopausal women.

Parameters	**Premenopausal Women n = 50**	**Postmenopausal Women n = 50**	**P-Value**
TWBC (x 10^9/l)	5.85±1.97	5.34±1.44	0.141
Neutrophils (x 10^9/l)	2.42±1.09	2.28±0.75	0.433
Lymphocytes (x 10^9/l)	2.93±1.08	2.71±0.81	0.239
Eosinophils (x 10^9/l)	0.42±0.31	0.29±0.27	0.018
Monocytes (x 10^9/l)	0.05±0.05	0.03±0.03	0.030
Platelets (x 10^9/l)	150.04±46.88	132.62±38.37	0.045
NLR	0.87±0.33	0.88±0.31	0.841
PLR	55.77±21.61	50.98±13.71	0.189
PT (Secs)	12.54±1.49	13.20±2.44	0.170
INR	0.97±0.12	1.01±0.19	0.170
APTT (Secs)	28.18±5.56	29.06±5.41	0.246
RPV (mPa/s)	1.59±0.10	1.74±0.17	0.001

Key: **TWBC** = total white blood cell count, **NLR** = neutrophil-to-lymphocyte ratio, **PLR** = platelet to lymphocyte ratio, **PT** = prothrombin time, **INR** = international normalized ratio, **APTT** = activated partial thromboplastin time, **RPV** = relative plasma viscosity.

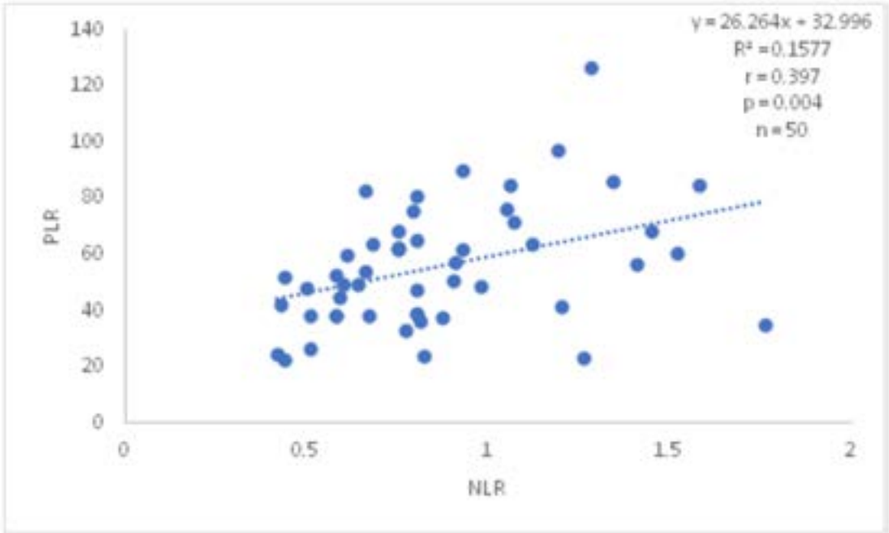

Figure 1. Positive correlation between NLR and PLR in premenopausal women

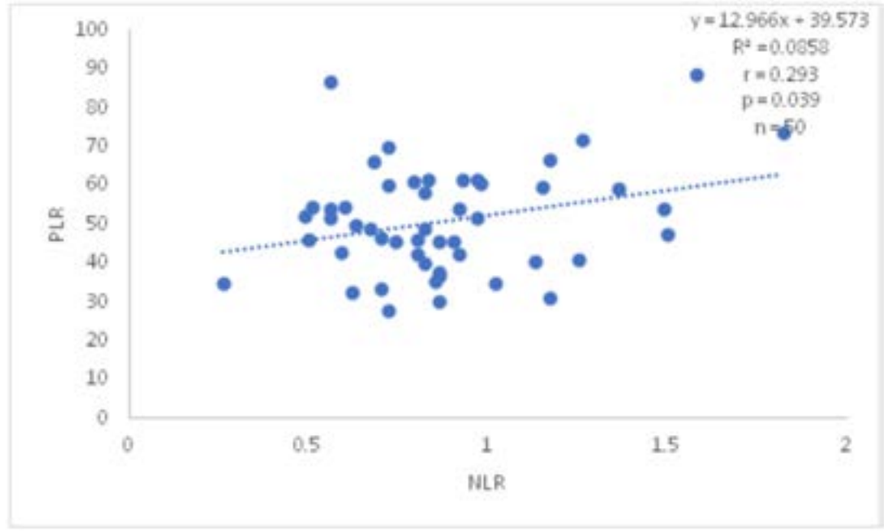

Figure 2. Positive correlation between NLR and PLR in Postmenopausal women

Conclusion

Inflammatory and thrombotic parameters are largely comparable in apparently healthy adult females irrespective of their reproductive phase. However, eosinophil, monocyte and platelet counts were observed to be significantly higher in premenopausal women compared to postmenopausal women.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Paramo JA, Lecumberri R. New mechanisms in vein thrombosi: immunothrombosis. Mid. Clin. 2019; 153: 78-81
2. Engelmann B, Massberg S. Thrombosis as an intravascular effector of innate immunity. Nat. Rev. Immunol. 2012; 13: 34-35.
3. Akwiwu EC, Edem MS, Okpokam DC, Akpotuzor JO, Anyanwu SO. Prediabetes and Endothelial Involvement among Apparently Healthy Persons. Tropical Journal of Natural Product Research 2023; 7(2): 2468-2471.
4. Stark K, Massberg S. Interplay between inflammation and thrombosis in cardiovascular pathology. Nat. Rev. Cardiol. 2021; 18: 666-682.
5. Akwiwu EC, Onukak EE, Isong IK, Akpotuzor JO, Bassey IE, Okafor AO. Crisis frequency and associated changes in platelet parameters among steady state sickle cell subjects. New Zealand Journal of Medical Laboratory Science 2020; 74: 91-94.
6. Akpan PA, Akwiwu EC, Njar VE, Odibu BE. Leucocyte Counts and Derivatives as Inflammatory Indicators in Active Tuberculosis. Tropical Journal of Natural Product Research 2023; 7(5): 3038-3041.
7. Udosen JE, Akwiwu EC, Njar VE, Akpotuzor DU, Abnimye DA, Akpotuzor JO. Selected Biomarkers of Coagulation Disturbance in Newly Diagnosed Breast Cancer Patients. Sokoto Journal of Medical Laboratory Sciences 2023: 8 (1) 60-64.
8. Goodman DA, Goodman CB, Monk JS. Use of the neutrophil:lymphocyte ratio in the diagnosis of appendicitis. Am Surg. 2012; 61:257–259.
9. Wu Q, Hu T, Zheng E, Deng X, Wang Z. Prognostic role of the lymphocyte-to-monocyte ratio in colorectal cancer. Medicine (Baltimore). 2017; 96(22): e7051.
10. Goto W, Kashiwagi S, Asano Y, Takada K, Takahashi K, Hatano T. Predictive value of lymphocyte-to-monocyte ratio in the preoperative setting for progression of patients with breast cancer. BMC Cancer 2018; 18: 1137.
11. Gasparyan AY, Ayvazyan L, Mukanova U, Yessirkepov M, Kitas GD. The platelet-to-lymphocyte ratio as an inflammatory marker in rheumatic diseases. Annals of laboratory medicine 2019; 39(4): 345-357.
12. Akwiwu EC, Ukpabi SA, Akpotuzor JO. Utility of Blood Cell Count Ratios as Biomarkers of Venous Thromboembolism Among Women on Oral Contraceptives. Journal of Medical Laboratory Science 2022; 32 (1): 34-40.
13. de Jager CP, van Wijk PT, Mathoera RB, de Jongh-Leuvenink J, van der Poll V, Wever PC. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit Care 2010; 14:R192.
14. Jeon Y, Lee WI, Kang SY. Neutrophil-to-Monocyte-Plus-Lymphocyte Ratio as a Potential Marker for Discriminating Pulmonary Tuberculosis from Nontuberculosis Infectious Lung Disease. Laboratory Medicine. 2019; 50(3): 286-291.
15. Kurtul A, Ornek E. Platelet to Lymphocyte Ratio in Cardiovascular Diseases: A Systematic Review. Angiology. 2019; 70(9): 802-818.
16. Abunimye DA, Akwiwu EC, Anyanwu SO, Onukak EE, Akpotuzor JO. Selected Inflammatory and Thrombotic Indicators among persons living with HIV infection in Southern Nigeria. African Journal of Laboratory Haematology and Transfusion Science 2022; 1 (2): 173-179.
17. Udosen JE, Akwiwu EC, Akpotuzor DU, Akpotuzor JO. Blood Cell Count Ratios in Post-Operative Breast Cancer Patients on Chemotherapy. African Journal of Laboratory Haematology and Transfusion Science 2022; 1 (1): 70-76.
18. Nakada D, Oguro H, Lavi BP, et al. Oestrogen increases haematopoietic stem cells self-renewal in females and during pregnancy. Nature. 2014; 505(7484): 555-558.
19. Agacayak E, Goruk NY, Kusen H. Role of inflammation and oxidative stress in etiology of primary ovarian insufficiency. Turkish journal of Obstetrics and Gynecology 2016; 13(3): 109-115.
20. DasGupta D. Is menopausal status related to women's attitudes toward menopause and aging. Women health Journal 2017; 57(3): 311-28.
21. Chakraborty B, Byemerwa J, Krebs T, Lim F, Chang CY, McDonnell DP. Estrogen Receptor Signaling in the Immune System. Endocr Rev. 2023; 44(1): 117-141.
22. Artham S, Chang CY, McDonnell DP. Eosinophilia in cancer and its regulation by sex hormones. Trends Endocrinol Metab. 2023; 34(1): 5-20.
23. Pepe G, Locati M, Torre SD et al. The estrogen-macrophage interplay in the homoastasis of the female reproductive tract. Human Reproduction Update 2018; 24(6): 652-672.
24. Butkiewicz AM, Kemona H, Dymicka-Piekarska V, Matowicka-Kama J. Does menopause affect thrombopoiesis and platelet activation? Przegl Lek. 2006; 63(12): 1291-1293.
25. Korkmaz H, Arslanca T, Tekin E, Kayabasi B, Akbulut KG. Evaluation of the relationship between plasma viscosity and selected menopausal symptoms using the Menopause Rating Scale. Menopause 2022; 29(9): 1071-1076.

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