Association of Platelet Count and Platelet Indices with Stages of Women Breast Cancer in Yola, Nigeria

Abstract

Background/Objective: Platelets are involved in mechanisms that promote tumor growth. Platelet indices are markers of platelet activities in cancer. Platelet indices includes: mean platelet volume (MPV), platelet distribution width (PDW), Plateletocrit (PCT), Platelet large cell ratio (P-LCR). This study aims to evaluate platelet count and platelet indices at different stages of women breast cancer in Yola.

Materials and Methods: 143 women participated in this study. Platelet count and platelet indices were determined using Sysmex XP 300 hematology analyzer.

Results: Mean platelet count in women with stage 0/1, 2, and 3/4, was 207±23.09 x 10^9/l, 113± 14.58 x 10^9/l and 412±12.50 x 10^9/l respectively. While mean PDW in women with stage 0/1, 2, and 3/4 breast cancer was 11.9 ±0.21fl, 13.1 ±1.1fl and 12.1 ±0.30fl respectively. MPV of women with stage 0/1, 2, and 3/4 breast cancer was 12.0 ± 1.20fl, 13.9 ± 0.26fl and 14.4 ± 0.88fl respectively. The mean P-LCR of women with stage 0/1 breast cancer was 32.4 ± 0.88% while P-LCR of those with stage 2 and 3/4 breast cancers was 21.8 ± 1.64% and 19.3 ± 1.15% respectively. Mean PCT of women on stage 0/1, 2, 3/4 was 0.23 ± 0.13%, 0.12 ± 1.02% and 0.29 ± 0.20% respectively.

Conclusion: Platelet counts and platelet indices vary with stages of breast cancer. Pattern of MPV variations indicates that MPV can be used as indices to measure platelet activation, tumor metastasis/invasion and inflammatory processes in women with breast cancer in Yola Nigeria.

Keywords: Platelet count; Platelet indices; Breast Cancer

Abbreviations: MPV: Mean Platelet Volume; PDW: Platelet Distribution Width; PCT: Plateletocrit; P-LCR: Platelet Large Cell Ratio

Introduction

Platelets are anucleated cells derived from megakaryocytes [1]. Platelets are multifunctional in nature and apart from playing a key role in hemostasis processes [2], platelets are also involved in mechanisms that promote tumor growth and metastasis [3,4]. Platelets secrete various growth factors and cytokines that promote angiogenesis, tumor growth, invasion and metastasis of cancer cells either directly or indirectly [5]. There are reports that thrombocytosis contributes to cancer metastasis [6-8]. In women with breast cancer, an increased circulating platelet is associated with poor cancer prognosis [9,10], and the ability of breast tumor cells to induce platelet aggregation correlates with their metastatic potential [11]. Studies in breast cancer models have also shown that direct interaction between breast cancer cells and platelets results in the activation of TGF-β (transforming growth factor-beta) signaling pathway, which promotes metastasis, and invasion of cancer cell by inducing epithelial-to-mesenchymal transition and immunosuppression [12,13] and breast cancer cells have been shown to prepare platelets to release pro-angiogenic proteins which stimulate migration and proliferation of cancer cells [14]. Platelets also stimulate the release of pro-inflammatory cytokines [interleukin 1, 3, and 6] by cancer cells [15] to enhance cancer progression.

Platelet indices are part of routine automated full blood counts. Platelet indices includes:

i. Mean Platelet Volume (MPV), which is a measurement of average platelets size [16]

ii. Platelet Distribution Width (PDW), which is a measure of variability in platelet sizes

iii. Plateletocrit (PCT), which indicates the volume of circulating platelets in a unit volume of blood [17] and

iv. Platelet Large Cell Ratio (P-LCR) which is a good aid in differential diagnosis of conditions associated with abnormal platelet counts [18,19].

MPV also reflects platelet production rate and stimulation through the changes in platelet size since larger platelets are more metabolically and enzymatically active than smaller platelets [20]. MPV is a test parameter that may be useful in identifying patients with newly diagnosed invasive ductal breast carcinoma [21] and elevated MPV value is associated with other markers of platelet activity including: platelet aggregation, increased thrombomodulin synthesis and β-thromboglobulin release [22].
Available evidence have suggested an important role of platelet indices as a marker of disease activity in cancer and several inflammatory diseases [17,23,24] and increased MPV value has been reported to be associated with disease conditions such as: obesity [25] hypertension [26] diabetes mellitus [27] renal failure [28] and atrial fibrillation [29]. P-LCR is inversely related to platelet count and directly related to PDW and MPV [30]. There is also report on P-LCR suggesting that its prognostic value is similar to that of MPV [30].

Breast cancer is a common malignancy among women and a serious health problem with 400,000 new cases being diagnosed annually worldwide [31]. Breast cancer is often divided into stages usually expressed as a number on a scale of 0 through IV with stage 0 describing non-invasive cancers that remain within their original location and stage IV describing invasive cancers that have spread outside the breast to other parts of the body. Despite multi-approaches in therapeutic management of breast cancer, including surgical, chemotherapy and radiation therapy, breast carcinoma remains a big clinical challenge and platelet indices may be useful in managing patients with breast cancer [21]. In Yola like most part of Nigeria however, information regarding platelet and platelet indices at various stages of breast cancer is not yet fully studied and documented, this study therefore aims to evaluate platelet count and platelet indices in women at various stages of breast cancer in Yola Nigeria in other highlights the usefulness of platelet count and platelet indices in the clinical management of women with breast cancer in this locality.

Materials and Methods

This study was carried out at medical laboratory department of Federal Medical Center of Yola, in Northeast Nigeria. 143 subjects comprising of 74 women (with mean age of 59.06 ± 2.14 years) who were clinically diagnose of breast cancer and 69 clinically healthy women (with a mean age of 53.23 ± 6.11 years) participated in this study. All study participants with breast cancer were clinically diagnosed and were referred to the laboratory for evaluation before commencement of therapy. Other informations were retrieved from their medical records. Platelet count and platelet indices were determined using Sysmex XP 300 hematology analyzer. All analyses were performed according to the standard operational procedures.

Sample collection

Three milliliters of blood were aseptically collected through the antecubital vein of subjects and put in EDTA vacutainer that was placed in a hematology blood mixer for five minutes and the blood platelet indices determination was as follows: EDTA samples were put in EDTA vacutainer within one hour of collection. Platelet count and platelet indices for each subject were performed in blood sample put in EDTA vacutainer that was placed in a hematology blood mixer for five minutes and the blood cells were automatically counted through a probe fitted in the Sysmex XP 300 machine. After one minute, the results of platelet count with platelet indices were displayed automatically on color LCD screen on the machine.

Statistical analyses

Statistical analysis was performed using the SPSS computer software version 20.0 (IBM Chicago, IL, USA). Descriptive values were given as mean and standard error of mean. Categorical variables were expressed as the number of cases and the percentage value. The Student’s t-test was used to compare the means differences of the estimated parameters and all statistics was carried out at the probability level of 0.05.

Results

Table 1 shows the demographic character of the studied population, 17 (22.9%) of the women investigated were married while 09 (12.2%) were divorced and 12 (16.2%) were widows and 07 (09.5%) of the women in this study were primiparous (given birth once) while 02 (2.7%) of the women were Nulliparous (not given birth previously) and 15 (20.3%) of the women were multiparous (has given birth more than once) while 11 (14.9%) of the women were Multigravida (pregnant more than once) and 1.3% of the women were Nulligravida (not been pregnant previously).

| Parameters | Number Observed | Percentage Prevalence | P-value |
|------------|-----------------|-----------------------|---------|
| Age        | 59.06±2.14 years| 0.05                  |         |
| Married    | 17              | 22.90%                | 0.05    |
| Divorce    | 9               | 12.20%                | 0.05    |
| Widow      | 12              | 16.20%                | 0.05    |
| Primiparous| 7               | 9.50%                 | 0.05    |
| Nulliparous| 2               | 2.70%                 | 0.05    |
| Multiparous| 15              | 20.30%                | 0.05    |
| Multigravida| 11             | 14.90%                | 0.05    |
| Nulligravida| 1              | 1.30%                 | 0.05    |

Thirty-nine (52.7%) of cancer in women observed in this study were at the breast ducts region while 40.5% of the cancer occurs at the lobules region of the breast and 6.8% of the cancer occurred at the region between duct and lobules of the breast as shown in Table 2. In addition, 4.1% and 6.8% of cancer observed in the women were at stage 0 and 1 respectively while 36.5% were at stage 2 and stage 3 of breast cancer was seen in 44.6% of the studied population (Table 3). Stage 4 of breast cancer occurred in 8.0% of women. The mean platelet count in women with stage 0 and stage 1 was 207±23.09 x 10^3/l while the platelet count in women with stage 2 breast cancers was 113± 14.58 x 10^3/l and women with stage 3 and 4 breast cancers had mean platelet counts of 412±12.50 x 10^3/l (Table 4). The mean platelet distribution width (PDW) in women with stage 0 and 1 breast cancer was 11.9 ±0.21fl while the mean PDW of women with stage 2 breast cancer was 13.1 ±1.1fl and PDW of 14.1 ±0.30fl was

Citation: Etim EA, Emokpae MA, Ohwongho AC, Yusuf AA (2018) Association of Platelet Count and Platelet Indices with Stages of Women Breast Cancer in Yola, Nigeria. Hematol Transfus Int J 6(1): 00145. DOI: 10.15406/htij.2018.06.00145
seen in women with stage 3 and 4 breast cancer. Mean PDW of the control group was 11.5 ± 1.21fl. In addition, Mean platelet volume (MPV) also varies with stages of breast cancer. The MPV of women with stage 0 and 1 breast cancer was 12.0 ± 1.20fl while that of the control group was 09.4 ± 1.43fl and MPV of those on stage 2 breast cancer was 13.9 ± 0.26fl and women with stage 3 and 4 breast cancer had MPV value of 14.4 ± 0.08fl. The mean platelet large cell ratio (P-LCR) of women with stage 0 and 1 breast cancer was 32.4 ± 0.88% while the P-LCR of those with stage 2 breast cancer was 21.8 ± 1.64% and P-LCR of 19.3 ± 1.13% was seen in women with stage 3 and 4 breast cancer. However, the mean plateletcrit (PCT) of 0.23 ± 0.13% was seen in women with stage 0 and 1 breast cancer while women with stage 2 breast cancer had a mean plateletcrit of 0.12 ± 1.02% and mean PCT of 0.29 ± 0.20% was seen in women with stage 3 and 4 breast cancer while the PCT of the control group was 0.31 ± 0.11%.

Table 2: Region of cancer in the Breast Observed.

| Region of Cancer in the Breast | Number Observed | Percentage Prevalence | p-value |
|-------------------------------|-----------------|-----------------------|---------|
| Ducts                         | 39              | 52.70%                | 0.05    |
| Lobules                       | 30              | 40.50%                | 0.05    |
| between duct and lobules      | 5               | 6.80%                 | 0.05    |

Table 3: Stages of Breast Cancer Observed in the Study Population.

| Stages of Breast Cancer | Number Observed | Percentage Prevalence | p-value |
|-------------------------|-----------------|-----------------------|---------|
| Stage 0                 | 3               | 4.10%                 | 0.05    |
| Stage 1                 | 27              | 6.80%                 | 0.05    |
| Stage 2                 | 33              | 36.50%                | 0.05    |
| Stage 3                 | 5               | 44.60%                | 0.05    |
| Stage 4                 | 6               | 8.00%                 | 0.05    |

Discussion

Platelet and platelet indices at various stages of breast cancer in women was evaluated in this study. The stages of breast cancer when the patients reported to the hospital were 4.1% and 6.8% at stage 0 and stage 1 respectively while 36.5%, 44.6% and 8.0% were at stage 2, 3 and 4 respectively. This indicates that a small portion (4.1 to 6.6%) of the studied group reported to the hospital at an early stage of breast cancer while large proportion (36.5 to 44.6%) reported late to the hospital at stages 3 and 4. This may be due to lack of knowledge of disease signs, symptoms, progression and high patronage of alternative and folkloric sources of medical treatment in this locality.

Changes in platelet count and platelet indices were observed to vary with different stages of breast cancer. The changes in platelet indices and platelet counts in various stages of breast cancer in this study is due to interaction between platelet and malignant cells [5,20]. Higher circulating platelet count was seen in women with stage 3 and 4 breast cancer than in women with stage 0 and 1 breast cancer (Table 2) this is because cancer cells (which increases with stages of cancer) have been known to stimulate platelet proliferation [32] and this also explains the high platelet count observed in patients with later (higher) stage of breast cancer compare to that of the control group. High platelet count in cancer was also observed in earlier study by Taucher et al. [9] and Sierko et al. [10] In addition, adequate platelet count seen in most stages of cancer is believed to promote the mechanism that facilitates the progression of breast cancer [11]. MPV was observed to increases with increase in cancer stage in this present study it is believed that, platelet size as reflected by MPV do increases in direct proportion to breast cancer progression. MPV value can also reflect the level of invasiveness of cancer cell [21] and high MPV is an indices of inflammation [17,23] it therefore goes to show that higher MPV value (than that of control observed in this study) may indicates high level of invasiveness and inflammatory processes in women with breast cancer and this inflammatory processes tends to increase as the stages of breast cancer increases. In addition, MPV value is a pointer to level of platelet function and activation [16] hence, increase in MPV implies increase platelet activation in this group of patients.

The mean P-LCR value was increased in cancer stage 0 and 1 but reduces in breast cancer stage 3 and 4. An increase P-LCR with increase MPV in stage 0 and 1 indicates that P-LCR may have a similar diagnostic value as MPV [30] in early stage of breast cancer.
cancer. Since PDW is a measure of platelet volume heterogeneity [33] it goes to show that slightly high PDW value seen in stage 2, 3, and 4 cancer reflects increase heterogeneity in platelet volume and size in these stages of breast cancer in women.

Conclusion

Platelet count and platelet indices vary at different stages of women breast cancer. The Pattern of variation in values of MPV and P-LCR at stage 0, 1, 2 of breast cancer may indicate that these platelet indices may be used as marker of platelet activation, tumor progression and inflammation in women with breast cancer. It is believed that information obtained from this study may help improve clinical management of women with various stages of breast cancer in this locality.

Author’s Contribution

Emmanuel Asuquo Etim assisted in research design, article writing, data generation and sample analysis. Abdulaleem Adebayo Yusuf assisted in research design, sample analysis. Mathias Abiodun Emokpae assisted literature review, editing and article writing. Adjebuko Collins Ohwonigho assisted in literature review and Data analysis.

Acknowledgement

The author wishes to appreciate all the subjects included in this study for their cooperation. We are also grateful to management and staffs of Federal Medical center Yola for playing a key role toward the success of this study. The study was sponsored by the authors, the equipment used was provided by the laboratory in which this work was done.

Conflict of Interest

There is no conflict of interest regarding this work among the authors.

References

1. George JN (2000) Platelets. Lancet 355(9214): 1531-1539.
2. Berger S (1970) Platelet function: A review. I. normal function. Can Med Assoc J 102(12): 1271-1274.
3. Menter DG, Tucker SC, Kopets S, Sood AK, Crisman JD, et al. (2014) Platelets and cancer: A causal or causal relationship: Revisited. Cancer Metastasis Rev 33(1): 231-269.
4. Franco AT, Corken A, Ware J (2015) Platelets at the interface of thrombosis, inflammation, and cancer. Blood 126(5): 582-588.
5. Yan M, Juratz P (2016) The role of platelets in the tumor microenvironment: From solid tumors to leukemia. Biochim Biophys Acta 1863(3): 392-400.
6. Nash GE, Turner LF, Scully MF, Kakkar AK (2002) Platelets and cancer. Lancet Oncol 3(7): 425-430.
7. Gay LJ, Felding-Habermann B (2011) Contribution of platelets to tumour metastasis. Nat Rev Cancer 11(2): 123-134.
8. Stone RL, Nick AM, McNeish IA, Balkwill F, Han HD, et al. (2012) Paraneoplastic thrombocytosis in ovarian cancer. N Engl J Med 366(7): 610-618.
9. Taucher S, Salat A, Grant M, Kwansy W, Milneritsch B, et al. (2003) Impact of pretreatment thrombocytosis on survival in primary breast cancer. Thromb Haemost 89(6): 1098-1106.
10. Sierko E, Wojtulikiewicz MZ (2004) Platelets and angiogenesis in malignancy. Semin in Thromb Hemost 30(1): 95-108.
11. Alonso-Escolano D, Strongin AY, Chung AW, Deryugina EI, Radomski MW (2004) Membrane type-1 matrix metalloproteinase stimulates tumour cell-induced platelet aggregation: role of receptor glycoproteins. Br J Pharmacol 141(2): 241-252.
12. Labelle M, Begum S, Hynes RO (2011) Direct signalling between platelets and cancer cells induces an epithelial-mesenchymal-like transition and promotes metastasis. Cancer Cell 20(5): 576-590.
13. Drabich Y, ten Dijke P (2011) TGF-beta signalling in breast cancer cell invasion and bone metastasis J Mammary Gland Biol Neoplasia 16(2): 97-108.
14. Battinelli EM, Markens BA, Italiano JE (2011) Release of angiogenesis regulatory proteins from platelet alpha granules: modulation of physiologic and pathologic angiogenesis. Blood 118(5): 1359-1369.
15. Burygo D, Wenz F, Groden C, Brockmann MA (2012) Tumor-platelet interaction in solid tumors. Int J Cancer 130(12): 2747-2760.
16. Nassaji M, Gharahmanfard F, Mirmohammadkhani M, T Tamadon MR, Manoochehrhi S (2014) Mean platelet volume and other platelet indices in adults patients with acute pyelonephritis. Asian J Pharm 4(3): 327-331.
17. Leader AI, Perry D, Lishner M (2012) Are platelet volume indices of clinical use? A multidisciplinary review. Ann Med 44(8): 805-16.
18. Babu E, Basu D (2004) Platelet large cell ratio in the differential diagnosis of abnormal platelet counts. Indian J Pathol Microbiol 47(2): 202-205.
19. Buttarello M, Plebani M (2008) Automated blood cell counts: state of the art. Am J Clin Pathol 130(1): 104-116.
20. Kannar V, Raja V, Suresh TN (2017) Evaluation of platelet indices in oral squamous cell carcinoma. Clin Cancer Investig J 6(1): 40-43.
21. Manta S, Kostakis ID, Machains N, Markopoulos C (2016) White blood cell and platelet indices as prognostic markers in patients with invasive ductal breast carcinoma. Oncol Lett 12(2): 1610-1614.
22. Bath PM, Butterworth R (1996) Platelet size: measurement, physiologic and vascular disease. Blood Coagul Fibrinolysis 7(2): 157-161.
23. Geyhazy AV, Ayazyan L, Mikhailidis DP, Kitas GD (2011) Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 17(1): 47-58.
24. Grieshammer M, Bangerter M, Sauer T, Wennauer R, Bergmann L, et al. (1999) Aetiology and clinical significance of thrombocytosis: analysis of 732 patients with an elevated platelet count. J Intern Med 245(3): 295-300.
25. Kalay N, Dogdu O, Koc F, Yaliloglu M, Arcic I, et al. (2012) Hematologic parameters and angiographic progression of coronary atherosclerosis. Angiology 63(3): 213-217.
26. Kanabarab M, Dogan A, Turkdogan AK, Kapci M, Duman A, et al. (2014) Mean platelet volume is increased in patients with hypertensive crises. Platelets 25(6): 423-426.
27. Lippi G, Salvagno GL, Nouvenne A, Meschi T, Borghi L, et al. (2015) The mean platelet volume is significantly associated with higher glycated hemoglobin in a large population of unselected outpatients. Prim Care Diabetes 9(3): 226-230.
Association of Platelet Count and Platelet Indices with Stages of Women Breast Cancer in Yola, Nigeria

28. Uçar H, Gür M, Koyunsever NY, Şeker T, Türkoğlu C, et al. (2014) Mean platelet volume is independently associated with renal dysfunction in stable coronary artery disease. Platelets 25(4): 274-278.

29. Tekin G, Tekin YK, Sivri N, Yetkin E (2013) Mean platelet volume in patients with nonvalvular atrial fibrillation. Blood Coagul Fibrinolysis 24(5): 537-539.

30. Gawlita M, Wasilewski J, Osadnik T, Regula R, Bujak K, et al. (2015) Mean platelet volume and platelet-large cell ratio as prognostic factors for coronary artery disease and myocardial infarction. Folia Cardiologica 10(6): 418-422.

31. Siegel R, Ma J, Zou Z, Jemal A (2014) Cancer statistics. CA Cancer J Clin 64(1): 9-29.

32. Boukerche H, Berthier-Vergnes O, Penin F, Tabone E, Lizard G, et al. (1994) Human-melanoma cell-lines differ in their capacity to release adp and aggregate platelets. Br J Haematol 87(4): 763-772.

33. Cui MM, Li N, Liu X, Yun ZY, Niu Y, et al. (2017) Platelet distribution width correlates with prognosis of non-small cell lung cancer. Sci Rep 7(1): 3456.