RESEARCH ARTICLE

Editorial Process: Submission:05/26/2025 Acceptance:01/15/2026 Published:01/21/2026

Platelet Indices as a Biomarker in Distinguishing Benign and Malignant Breast Lesions

Oshan Shrestha[1]*, Swati Jha[1], Barsha Deo[1], Bhaktaraj Majhi[1], Ganesh Devkota[2], Hari Prasad Dhakal[3]

Abstract

Background: Platelets possess an important biological role at several stages of various malignant diseases. Platelet activation, as manifested by platelet indices, could help establish them as a diagnostic non-invasive biomarker for use in distinguishing benign and malignant breast lumps. **Objectives:** To compare various platelet indices in patients with different categories of breast lesions and among different cytological or histological grades of breast carcinoma. **Methods:** This was a prospective cross-sectional analytical study conducted in the Department of Pathology at Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. It included 93 cytologically and histopathologically proven cases of breast lesions over a period of 9 months from September 2024 to May 2025. Blood samples from all 93 patients and 31 healthy controls were assessed for various parameters. The ANOVA test was used to compare different platelet indices across different categories and grades of breast lesions. **Result:** Statistically significant differences in platelet counts, mean platelet volume, platelet-large cell ratio and platelet-lymphocyte ratio were observed when comparing the control group with the malignant group ($p<0.001$ in all indices), the non-neoplastic group with the malignant group ($p<0.001$ in all indices), and the benign group with the malignant group ($p<0.001$ in all indices). Platelet distribution width additionally showed significant differences between non-neoplastic group and benign group (p value 0.008). Amongst the various grades within malignant group, differences in platelet indices were not significant. **Conclusion:** Malignant breast tumors are associated with higher levels of platelet activation and systemic inflammatory response, which are reflected in altered platelet parameters. Platelet indices may assist in distinguishing between malignant and non-malignant lesions, but are less reliable in grading the malignancy.

Keywords: Blood Platelets- Breast Neoplasms- Platelet activation

Asian Pac J Cancer Prev, **27 (1)**, 157-161

Introduction

Breast cancer is the most common cancer in women and carries a significant disease burden. It accounted for around 2.3 million new cases and 670,000 deaths worldwide in 2022 [1]. Platelets have been shown to possess an important biological role at several stages of various malignant diseases, such as promoting angiogenesis, tumor cell proliferation, invasiveness, and metastasis [2, 3]. Parameters related to platelet size and number reflect platelet activity and named as platelet indices. Owing to the activation of platelets by tumor cells as well as the established role of platelets in promoting tumor cell development, these indices are altered in malignant conditions. The indices include Platelet Count (PC), Platelet Distribution Width (PDW), Mean Platelet Volume (MPV), Platelet-Large Cell Ratio (P-LCR) and Platelet to Lymphocyte ratio (P/L) [4]. Other factors like platelet clumping, pregnancy, viral infections, chronic inflammatory conditions, hypersplenism and bone marrow disorders including aplastic anemia, myeloproliferative neoplasms, myelodysplastic neoplasms may also alter the platelet indices [4, 5]. Various studies have shown that high platelet count correlated with poor prognosis in patients with malignancies of colon, lung, stomach, kidneys, prostate, endometrium, ovary and in malignant mesothelioma [6–11]. Platelet distribution width analysis has also been exploited to differentiate benign and malignant thyroid lesions [12].

Many blood-based sources of biomarkers, such as plasma, serum and circulating RNA/DNA, tumor cells, or exosomes/microparticles, have been exploited in the search for the ideal biomarker allowing detection of cancer at its earliest stages. There however exists substantial hurdles that must be overcome to fully realize its potential [13]. Platelet indices can be easily recorded from a routine

*[1]Department of Pathology, Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. [2]Department of Radiodiagnosis, Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. [3]Department of Pathology and Laboratory Medicine, Nepal Cancer Hospital and Research Centre, Lalitpur, Nepal. *For Correspondence: oshanpgi@gmail.com*

complete blood count (CBC) analysis which is a relatively much cheaper and minimally invasive blood test. There is however no study till date that has assessed these platelet indices to distinguish benign from a malignant breast lump before confirmation by cytological or histopathological techniques.

The present study aimed to compare platelet indices among 4 groups i.e., benign non-neoplastic breast lesions, benign neoplastic breast lesions, malignant breast lesions and age matched healthy controls. A secondary aim was to compare platelet indices among different cytological or histological grades in cases with malignant breast lesions.

Materials and Methods

This was a cross-sectional analytical study conducted in Department of Pathology at Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. It included cytologically and histopathologically proven cases of breast lesions over a period of 9 months from September 2024 to May 2025. Ethical approval was obtained from the Institutional review committee of the same institute (Reference no. 65/2024). Written informed consents were obtained from all participants.

The study population included 124 females; 93 of these with palpable breast lumps and 31 composed of normal age matched female controls, all with no hematological or other neoplastic disorders. The sample size (n=31) was estimated using Cochran's formula i.e. n=z2pq/d2 where the prevalence (p=0.09) was taken from the total malignant cases in last year that was 40 amongst 426 total breast lumps investigated. Margin of error (d=0.01) was taken at 10% and the z-value was 1.96 with confidence level set at 95%. Exclusion criteria included patients on anti-platelet drugs or non-steroidal anti-inflammatory drugs in last 12 days, active smokers or patients with any known platelet disorders. The 12 days cut-off was set since the average lifespan of platelets in circulation is 7 to 10 days [14].

The breast lumps were diagnosed on Pap and Giemsa-stained Fine needle aspiration cytology (FNAC) smears or on Haematoxylin and Eosin-stained histopathology slides whichever was applicable. The malignant cases in cytology were further graded by Robinson's cytological grading system [15]. On histopathology specimens, the malignant cases were graded using Nottingham's modified Bloom-Richardson method [16].

Platelet indices including PC, PDW, MPV, PLCR and P/L were noted from values obtained by Hematology Sysmex XN-550 analyser using impedance method and fluorescence flow cytometry technology.

Statistical analysis

Statistical Package for the Social Science (SPSS) version 16 (IBM, Armonk, NY, USA) was used for statistical analysis. All data were expressed as mean ± standard deviation (SD). Normality testing of the data in numerical variables was done using Shapiro-Wilk test. Test for homogeneity of variances was done using Levene's test. Dependent variables like PC, MPV, PDW, P-LCR, and P/L were compared with different categories and/or grades of breast lesions as well as normal controls using Analysis of variance (ANOVA) test. A threshold of $p < 0.05$ was considered statistically significant. Post Hoc analysis was done with Tukey's HSD (Honestly Significant Difference) test or Dunnett's T3 to compare differences between the different groups.

Results

Among the study population, 93 had breast lumps of which 78 were diagnosed on FNAC and 15 by histopathological study. The mean of PC, MPV, PDW, PLCR and P/L in the 3 sub-groups with different categories of breast lump and control group with no breast lump are shown in Table 1. These indices showed increment in values as the categories changed from non-neoplastic lump to benign neoplasm to malignant groups in that order. For example, mean platelet count in the non-neoplastic lump category was 2,00,161/cu.mm. while it was 2,33,865/cu.mm and 3,98,226/cu.mm. in benign and malignant categories respectively. Platelet to lymphocyte ratio was 81.9, 95.3 and 181.4 in non-neoplastic, benign and malignant lumps respectively.Values however did not show such homogenous difference amongst control and non-neoplastic lump groups.

Statistically significant differences in PC, MPV, PDW, PLCR and P/L were observed while comparing malignant group with control, non-neoplastic lump and benign neoplasm groups. In addition to this, PDW also showed statistically significant difference in benign versus non-neoplastic lump group (Table 2). No significant difference in any platelet indices was seen while comparing control group with non-neoplastic lump group and control group with benign neoplasm group. Likewise, except PDW, all other platelet indices did not show any significant difference while comparing non neoplastic group with benign neoplasm group. It was 11.1% in the non-neoplastic lump group and 13.4% in the benign neoplasm group

Within the malignant group, all the indices i.e., PC, MPV, PDW, PLCR and P/L were higher as the grades of malignancy increased i.e., it gradually increased from low grade to intermediate grade, and from intermediate grade to high grade. This difference was however not statistically significant (Table 3).

Table 1. Distribution of Different Platelet Indices among the 4 Sub-Groups

Category	PC ± SD (/cu.mm.)	MPV ± SD (fl)	PDW ± SD (%)	PLCR ± SD	P/L ± SD
Control (n=31)	222319 ± 60612	9.6 ± 1.6	11.9 ± 2.1	23.3 ± 5.1	80.8 ± 19.1
Non-neoplastic (n=31)	200161 ± 53700	9.6 ± 1.3	11.1 ± 1.3	26.8 ± 8.7	81.9 ±19.1
Benign neoplastic (n=31)	233864 ± 63040	10.6 ± 1.4	13.3 ± 3.0	27.4 ± 9.7	95.3 ± 15.7
Malignant (n=31)	398226 ± 90352	12.4 ± 1.1	18.7 ± 4.0	38.8 ± 7.8	181.4 ± 32.1

Table 2. Comparison of Platelet Indices amongst Groups with Breast Lumps.

Non-neoplastic vs Benign		
Platelet indices	Mean difference	p-value
PC	33703 ± 17365	0.217 [a]
MPV	0.9 ± 0.3	0.067 [b]
PDW	2.3 ± 0.7	0.008 [a]
PLCR	0.6 ± 2.3	1.000 [a]
P/L	13.5 ± 5.6	0.079 [b]
Non-neoplastic vs Malignant		
Platelet indices	Mean difference	p-value
PC	198065 ± 17365	<0.001 [a]
MPV	2.8 ± 0.3	<0.001 [b]
PDW	7.7 ± 0.7	<0.001 [a]
PLCR	12 ± 2.1	<0.001 [a]
P/L	99.5 ± 5.6	<0.001 [b]
Benign vs Malignant		
Platelet indices	Mean difference	p-value
PC	164361 ± 17365	<0.001 [a]
MPV	1.9 ± 0.3	<0.001 [b]
PDW	5.4 ± 0.7	<0.001 [a]
PLCR	11.4 ± 2.2	<0.001 [a]
P/L	86.1 ± 5.6	<0.001 [b]

P value <0.05 considered statistically significant; [a]ANOVA with post hoc Tukey HSD; [b] ANOVA with post hoc Dunnett T3

Table 3. Comparison of Different Platelet Indices between and Within Different Grades of Malignant Lumps

Platelet indices	p-value (ANOVA)
PC	0.073
MPV	0.337
PDW	0.071
PLCR	0.107
P/L	0.174

P value <0.05 considered statistically significant

Discussion

This study investigated the utility of platelet indices as potential biomarkers in distinguishing benign and malignant breast lesions, as well as their association with tumor grade within malignant cases. In this study, we revealed notable patterns in platelet indices distribution across the 4 groups studied. We demonstrated that among the control, non-neoplastic lump, benign neoplasm, and malignant groups, all measured platelet indices generally followed a consistent trend: values were lowest in the control group and gradually increased across non-neoplastic lump and benign neoplasm groups, reaching the highest levels in malignant cases.

Our results suggest a strong association between elevated PC and the presence of malignant breast lesions, consistent with prior research indicating a role of thrombocytosis in cancer progression and metastasis [17, 18].

Our findings in PC and MPV also aligns with the hypothesis that as tumor aggressiveness and biological activity increase, the interaction between tumor cells and the hematopoietic system may intensify, potentially contributing to elevated platelet production or reduced clearance [19]. A study by Hermansyah et al. had concluded that platelet counts is a potential hematological biomarker to predict histopathological grading in invasive breast cancers [20]. However, the absence of statistical significance in our study indicates that while there may be a biological gradient, larger sample sizes or further studies are required to confirm a consistent correlation.

Our findings suggest a possible association between elevated MPV and neoplastic transformation. Similar patterns have been reported in prior studies where patients with breast cancer demonstrated significantly higher MPV levels than those with benign conditions or healthy individuals [21–24].

Our observation in PLCR also align with previous studies suggesting that platelet indices, including P-LCR, are significantly elevated in various malignancies due to systemic inflammation and malignancies [25, 26].

Likewise, high P/L was also associated with poor overall survival and disease-free survival as observed in a meta-analysis performed by Zhu et al. in 2016 [27]. Similar result of elevated P/L being associated with poor overall survival was also seen in another meta-analysis performed on urinary bladder carcinomas [28]

Similar trend in PDW observed in our study also aligns with the biological understanding that neoplastic transformation is often associated with increased platelet activation as platelets and its microparticles plays role in tumor angiogenesis, thromboembolic events and interaction with other cells of the tumor microenvironment in neoplasms [19].

Unique to the PDW, our study suggests that it may be more sensitive in detecting early benign neoplastic changes compared to other platelet markers. Similar finding of statistically significant elevation of PDW in malignant thyroid nodules as compared to benign thyroid nodules was also noted in another study [12]. A study by Kurtoglu in endometrial lesions have however found significantly reduced PDW in the malignant endometrial lesions compared to benign ones [29]. This is likely because they have included cases with advanced endometrioid endometrial carcinoma where continuous platelet consumption and activation might have led to a more homogeneous population of platelets, thus lowering PDW.

In contrast, comparisons of platelet indices (except for PDW) between the control group versus non-neoplastic group, control group versus benign neoplastic group, and non-neoplastic versus benign neoplastic groups did not yield statistically significant differences. This lack of significance suggests that platelet indices may not be substantially altered in non-malignant breast conditions, underscoring the specificity of platelet activation in the context of malignancy.

Thus, the elevation in PC, MPV, PLCR and P/L appears

to be more specifically associated with malignant processes rather than with benign neoplastic or inflammatory breast changes.

Although all indices tended to increase with advancing tumor grade (from low to high), none of these intra-malignant group differences reached statistical significance, indicating that while platelet indices may assist in distinguishing between malignant and non-malignant lesions, they may be less reliable in grading the severity of malignancy. To the best of our knowledge, there are however no studies till date that looked into the variation of platelet indices amongst different breast cancer grades. The small subgroup sizes within different malignant tumor grades also might have limited statistical power to show significant differences in platelet indices, despite a consistent upward trend across grades.

In conclusion, this study showed that use of PC, MPV, PDW, PLCR and P/L might aid in distinguishing between malignant and non-malignant breast lesions. PDW in addition, is likely a potentially useful tool in differentiating even benign neoplasms from reactive or inflammatory lumps that are not neoplastic in nature.

Cross-sectional design of this study however restricts the ability to evaluate changes in platelet indices over time, limiting insights into their role in disease progression and treatment response. Although known factors influencing platelet indices were excluded, residual confounding from unmeasured variables such as subclinical inflammatory states, viral infections, or undiagnosed hematological conditions cannot be ruled out.

We advocate further studies with larger sample sizes and prospective designs, with adjustment for confounders, to validate these findings and explore their prognostic implications in breast cancer.

Author Contribution Statement

O.S. designed the research; summarized, and analyzed data; and wrote the paper. O.S. is also the corresponding author; H.D. contributed in research design, supervision and critical review of the manuscript and help approve the final version, S.J., B.D. and B.M. collected the data, and gave critique. G.D. helped in diagnostic procedures required for categorizing patient groups. All authors read and approved the final manuscript.

Acknowledgements

The authors would like to extend their gratitude to all the resident doctors and staffs in Department of Pathology, Nobel Medical College and Teaching Hospital, Biratnagar, Nepal.

Approval

Approved by Institutional review committee. It was a part of student thesis of Master in Medical Research Program.

Disclosure Statement

The authors report no conflicts of interest or relevant financial relationships to disclose.

Ethical Declaration

Approved by Institutional review committee of Nobel Medical College and Teaching Hospital, Biratnagar, Nepal.

Conflict of Interest

The authors report no conflicts of interest

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63. https://doi.org/10.3322/caac.21834.
2. Sabrkhany S, Kuijpers MJE, Oude Egbrink MGA, Griffioen AW. Platelets as messengers of early-stage cancer. Cancer Metastasis Rev. 2021;40(2):563-73. https://doi.org/10.1007/s10555-021-09956-4.
3. Schlesinger M. Role of platelets and platelet receptors in cancer metastasis. J Hematol Oncol. 2018;11(1):125. https://doi.org/10.1186/s13045-018-0669-2.
4. Pogorzelska K, Kręt owska A, Krawczuk-Rybak M, Sawicka-Żukowska M. Characteristics of platelet indices and their prognostic significance in selected medical condition - a systematic review. Adv Med Sci. 2020;65(2):310-5. https://doi.org/10.1016/j.advms.2020.05.002.
5. de Gaetano G, Santimone I, Gianfagna F, Iacoviello L, Cerletti C. Variability of platelet indices and function: Acquired and genetic factors. Handb Exp Pharmacol. 2012(210):395-434. https://doi.org/10.1007/978-3-642-29423-5_16.
6. Costantini V, Zacharski LR, Moritz TE, Edwards RL. The platelet count in carcinoma of the lung and colon. Thromb Haemost. 1990;64(4):501-5.
7. Ikeda M, Furukawa H, Imamura H, Shimizu J, Ishida H, Masutani S, et al. Poor prognosis associated with thrombocytosis in patients with gastric cancer. Ann Surg Oncol. 2002;9(3):287-91. https://doi.org/10.1007/bf02573067.
8. Symbas NP, Townsend MF, El-Galley R, Keane TE, Graham SD, Petros JA. Poor prognosis associated with thrombocytosis in patients with renal cell carcinoma. BJU Int. 2000;86(3):203-7. https://doi.org/10.1046/j.1464-410x.2000.00792.x.
9. Ribeiro M, Ruff P, Falkson G. Low serum testosterone and a younger age predict for a poor outcome in metastatic prostate cancer. Am J Clin Oncol. 1997;20(6):605-8. https://doi.org/10.1097/00000421-199712000-00015.
10. Gücer F, Moser F, Tamussino K, Reich O, Haas J, Arikan G, et al. Thrombocytosis as a prognostic factor in endometrial carcinoma. Gynecol Oncol. 1998;70(2):210-4. https://doi.org/10.1006/gyno.1998.5078.
11. Nakano T, Fujii J, Tamura S, Hada T, Higashino K. Thrombocytosis in patients with malignant pleural mesothelioma. Cancer. 1986;58(8):1699-701. https://doi.org/10.1002/1097-0142(19861015)58:8<1699::aid-cncr2820580820>3.0.co;2-b.
12. Li N, Fu S, Cui MM, Niu Y, Li B, Liu ZP, et al. Platelet distribution width and serum albumin levels for discrimination of thyroid cancer from benign thyroid nodules. Asian Pac J Cancer Prev. 2017;18(7):1773-7. https://doi.org/10.22034/apjcp.2017.18.7.1773.
13. Venetis K, Cursano G, Pescia C, D'Ercole M, Porta FM, Blanco MC, et al. Liquid biopsy: Cell-free DNA based analysis in breast cancer. J Liq Biopsy. 2023;1:100002. https://doi.org/10.1016/j.jlb.2023.100002.

14. Josefsson EC, Vainchenker W, James C. Regulation of platelet production and life span: Role of bcl-xl and potential implications for human platelet diseases. Int J Mol Sci. 2020;21(20). https://doi.org/10.3390/ijms21207591.
15. Robinson IA, McKee G, Nicholson A, D'Arcy J, Jackson PA, Cook MG, et al. Prognostic value of cytological grading of fine-needle aspirates from breast carcinomas. Lancet. 1994;343(8903):947-9. https://doi.org/10.1016/s0140-6736(94)90066-3.
16. Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: Experience from a large study with long-term follow-up. Histopathology. 1991;19(5):403-10. https://doi.org/10.1111/j.1365-2559.1991.tb00229.x.
17. Stone RL, Nick AM, McNeish IA, Balkwill F, Han HD, Bottsford-Miller J, et al. Paraneoplastic thrombocytosis in ovarian cancer. N Engl J Med. 2012;366(7):610-8. https://doi.org/10.1056/NEJMoa1110352.
18. Buergy D, Wenz F, Groden C, Brockmann MA. Tumor-platelet interaction in solid tumors. Int J Cancer. 2012;130(12):2747-60. https://doi.org/10.1002/ijc.27441.
19. Haemmerle M, Stone RL, Menter DG, Afshar-Kharghan V, Sood AK. The platelet lifeline to cancer: Challenges and opportunities. Cancer Cell. 2018;33(6):965-83. https://doi.org/10.1016/j.ccell.2018.03.002.
20. Hermansyah D, Al Anas M, Firsty NN, Siregar DR. High platelet count as a predicting factor of histopathological grading among invasive breast cancer individuals: A single centre experience from indonesia. Rep Pract Oncol Radiother. 2023;28(1):9-14. https://doi.org/10.5603/RPOR.a2023.0008.
21. Gu M, Zhai Z, Huang L, Zheng W, Zhou Y, Zhu R, et al. Pre-treatment mean platelet volume associates with worse clinicopathologic features and prognosis of patients with invasive breast cancer. Breast Cancer. 2016;23(5):752-60. https://doi.org/10.1007/s12282-015-0635-6.
22. Tanriverdi O, Menekse S, Teker F, Oktay E, Nur Pilanc K, Gunaldi M, et al. The mean platelet volume may predict the development of isolated bone metastases in patients with breast cancer: A retrospective study of the young researchers committee of the turkish oncology group (tog). J buon. 2016;21(4):840-50.
23. Divsalar B, Heydari P, Habibollah G, Tamaddon G. Hematological parameters changes in patients with breast cancer. Clin Lab. 2021;67(8). https://doi.org/10.7754/Clin.Lab.2020.201103.
24. Sun H, Yin CQ, Liu Q, Wang F, Yuan CH. Clinical significance of routine blood test-associated inflammatory index in breast cancer patients. Med Sci Monit. 2017;23:5090-5. https://doi.org/10.12659/msm.906709.
25. Çelik O, Laloğlu E, Çelik N. The role of platelet large cell ratio in determining mortality in covid-19 patients. Medicine (Baltimore). 2024;103(18):e38033. https://doi.org/10.1097/md.0000000000038033.
26. Lembeck AL, Posch F, Klocker EV, Szkandera J, Schlick K, Stojakovic T, et al. Large platelet size is associated with poor outcome in patients with metastatic pancreatic cancer. Clin Chem Lab Med. 2019;57(5):740-4. https://doi.org/10.1515/cclm-2018-0016.
27. Zhu Y, Si W, Sun Q, Qin B, Zhao W, Yang J. Platelet-lymphocyte ratio acts as an indicator of poor prognosis in patients with breast cancer. Oncotarget. 2017;8(1):1023-30. https://doi.org/10.18632/oncotarget.13714.
28. Wang X, Ni X, Tang G. Prognostic role of platelet-to-lymphocyte ratio in patients with bladder cancer: A meta-analysis. Front Oncol. 2019;9:757. https://doi.org/10.3389/fonc.2019.00757.
29. Kurtoglu E, Kokcu A, Celik H, Sari S, Tosun M. Platelet indices may be useful in discrimination of benign and malign endometrial lesions, and early and advanced stage endometrial cancer. Asian Pac J Cancer Prev. 2015;16(13):5397-400. https://doi.org/10.7314/apjcp.2015.16.13.5397.