

ORIGINAL RESEARCH

Significance of Red Cell Distribution Width to Platelet Count Ratio (RPR) in Patients with Breast Cancer

Pravallika Mallipeddi¹, Sowjanya Rakam², Venkata Sri Laxmi Chennupati³

¹Senior Resident, Department of pathology, Osmania Medical College/SRRIT&CD, Govt Fever Hospital, Hyderabad, Telangana, India.

²Assistant Professor, Department of Pathology, Gandhi Medical College/SRRIT&CD, Govt Fever Hospital, Hyderabad, Telangana, India.

³Senior Resident, Department of pathology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.

ABSTRACT

Background: Red cell distribution width (RDW) to platelet ratio (RPR) is a prognosticator in acute pancreatitis and myocardial infarction; however, the prognostic values of RDW and RPR in breast cancer have not been studied. This retrospective analysis of 50 breast cancer patients investigated the association between RDW and RPR and clinicopathological characteristics and prognosis, compared to platelet distribution width to platelet count ratio (PDW/P) which is a known independent prognostic factor in patients with breast cancer. **Aims and Objective:** Our study aimed to know significance of elevated RPR in breast cancer, to correlate the RPR with the clinicopathological characteristics of breast cancer (tumor grade, lymphatic spread, over expression of hormonal receptors and HER2 protein).

Materials & Methods: It was a Retrospective study. Patients with histologically confirmed breast cancer were included in study. Patients with heart failure / On dialysis/ Lacking the entire set of clinicopathological data were excluded in this study.

Results: RPR was higher in patients with breast cancer. RPR elevation was significantly correlated with high grade tumors, number of infiltrated lymph nodes and HER2 over expression.

Conclusion: Our study indicates that elevated preoperative RDW levels are indicative of tumor spread and progression of breast cancer. RPR is a cost-effective and novel biomarker which can help in assessing the microscopic grading of Breast cancer.

Keywords: RDW, Platelet, Breast cancer.

Corresponding Author: Dr Sowjanya Rakam, Assistant Professor, Department of Pathology, Gandhi Medical College/SRRIT&CD, Govt Fever Hospital, Hyderabad, Telangana, India.

INTRODUCTION

Breast cancer is the most common female cancer in the world.^[1] Red blood cell distribution width (RDW), an indicator of the variability in the sizes of circulating red blood cells. As tumour size increased, an extensive inflammatory reaction might be triggered which suppress erythrocyte maturation and accelerate reticulocytes causing elevated RDW.^[2] Platelets are associated with tumour growth and metastasis due to the release of growth factors. Red blood cell distribution width to Platelet Ratio (RPR) is regarded as an indicator of systemic inflammatory response and related to poorer survival among breast cancer patients.^[3] Therefore, the liquid biopsy is used in the early detection of cancer; however, its clinical use is still limited due to its uncertain role and high cost.^[4] Thus, there could be an urgent need to

establish simple and low-cost prognostic biomarkers for breast cancer using routine haematological parameters of the complete blood count.

Recently, it was demonstrated that platelet distribution width to platelet count ratio (PDW/P) was a significant prognostic factor in patients with breast cancer.^[5] Hence, the purpose of the present study was to investigate the prognostic value of the RDW and RPR in breast cancer patients, compared with PDW/P.

Aim & Objectives

- To study the significance of elevated RPR in breast cancer.
- To study association of RPR with the clinicopathological characteristics of breast cancer (Age, Tumor grade, Lymphatic spread, HER2 protein expression).

MATERIALS & METHODS

Type of the study: Retrospective study

Place of the study: Tertiary health centre.

Time period of the study: January 2018 and June 2019.

Sample size: 50 patients with histologically confirmed breast cancer.

Inclusion criteria:

- Patients with histologically confirmed breast cancer

Exclusion criteria:

- Patients with heart failure
- Patients on dialysis
- Lacking the entire set of clinicopathological data for this study.

Methods of Collection of Data

Two ml of EDTA anticoagulated blood were collected from 50 patients and processed through FX- 19T automated hematology analyzer.

The RPR was calculated by dividing the RDW by the platelet count ($\times 10^9/\mu\text{L}$).

Clinicopathological characteristics of breast cancer - Age, Tumor grade, Lymphatic spread, HER2 protein expression were retrieved.

RESULTS

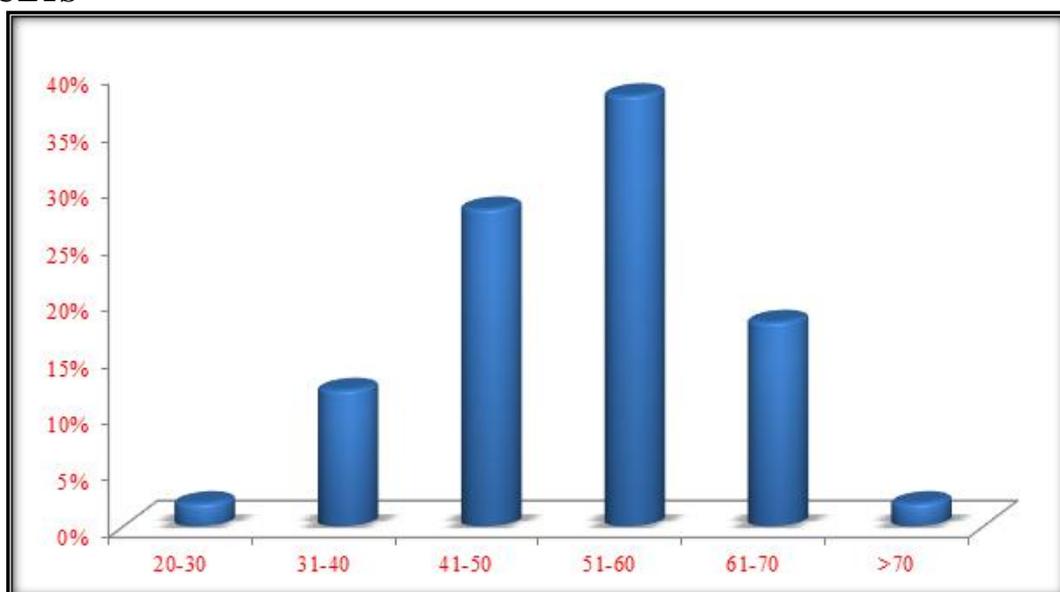


Figure 1: Age wise distribution of cases

In the present study Age: MEAN + SD 51.62 ± 9.54

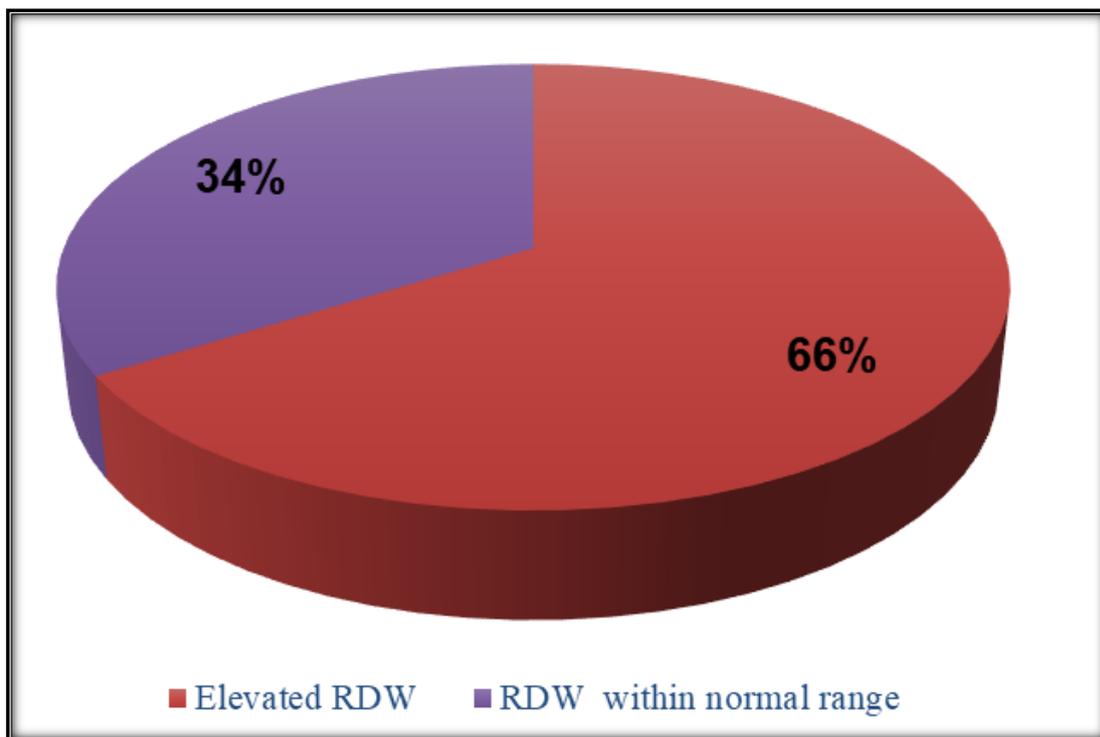


Figure 2: RDW DISTRIBUTION AMONG CASES

RDW : MEAN + SD 15.37 ± 3.48

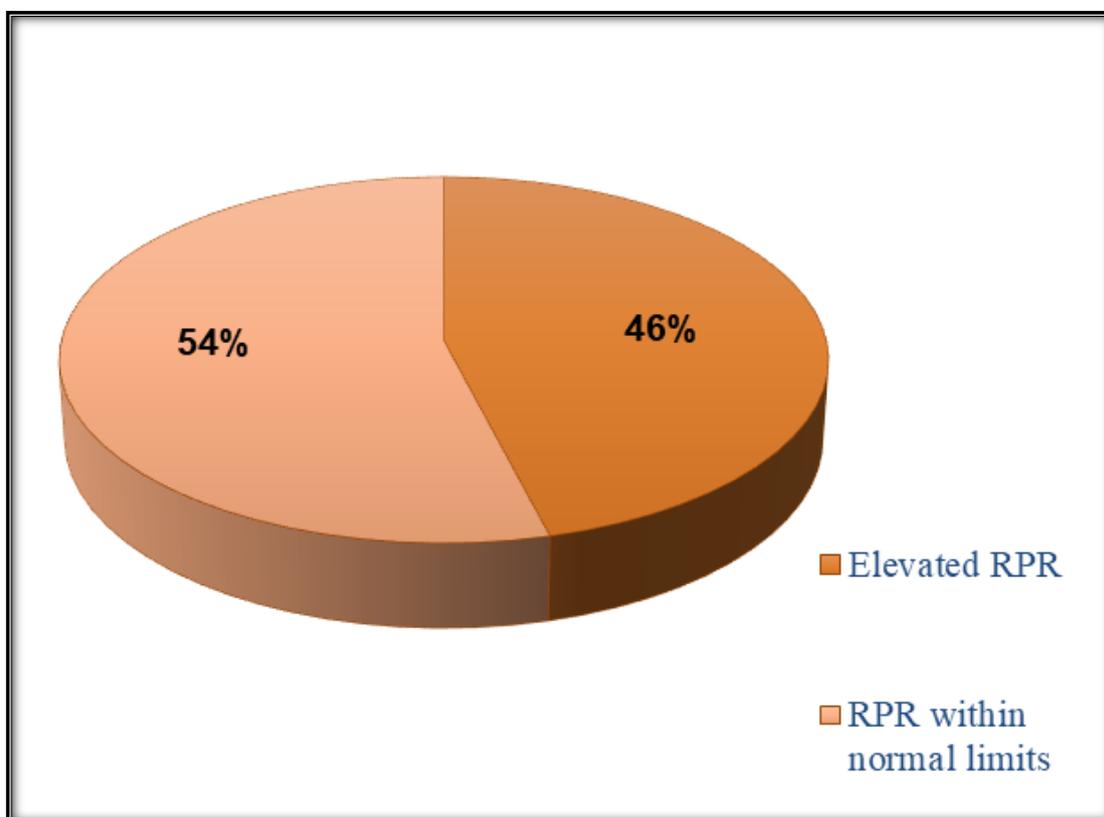


Figure 3: RPR Distribution Among Cases

RPR: MEAN + SD 0.051 ± 0.018

Table 1: Variuos tumors distributions among all cases

RDW	Low Grade Tumours	High Grade Tumours	Total	Chi square	P value
< 13.7	5	12	17	5.081	0.024, Significant
>13.7	2 (7%)	31 (93%)	33 (100%)		
Total	7	43	50		
RDW	Metastasis negative	Metastasis positive	Total	Chi square	P value
<13.7	12	5 (29%)	17	0.241	0.623, non-Significant
>13.7	21	12 (71%)	33		
Total	33	17 (100%)	50		
RDW	Age<50	Age>50	Total	Chi square	P value
<13.7	4	13	17	2.911	0.08, non-Significant
>13.7	16 (49%)	17 (51%)	33 (100%)		
Total	20	30	50		
RDW	HER 2 Negative	HER 2 Positive	Total	Chi square	P value
<13.7	11	6	17	0.08	0.77, non-Significant
>13.7	20 (60%)	13 (40%)	33 (100%)		
Total	31	19	50		

Table 2: Total RPR

RPR	Low grade tumours	High grade tumours	Total	Chi square	P value
< 0.05	6	21	27	2.917	0.08, non-Significant
>0.05	1(4%)	22(96%)	23(100%)		
Total	7	43	50		
RPR	Metastasis negative	Metastasis positive	Total	Chi square	P value
< 0.05	19	8(47%)	27	1.156	0.28, non-Significant
>0.05	14	9(53%)	23		
Total	33	17(100%)	50		
RPR	Age<50	Age>50	total	Chi square	P value
< 0.05	9	18	27	1.087	0.29, non-significant
>0.05	11 (49%)	12 (52%)	23 (100%)		
Total	20	30	50		
RPR	HER 2 Negative	HER 2 Positive	total	Chi square	P value
< 0.05	17	10	27	0.02	0.879, non-significant
>0.05	14 (60%)	9 (40%)	23 (100%)		
Total	31	19	50		

DISCUSSION

To the best of our knowledge, this is the first study to demonstrate that the elevated RPR could be an independent risk factor for prognosis in breast cancer patients and is more powerful than PDW/P as a prognostic factor. RPR was recognised as a strong predictor of the severity of fibrosis and cirrhosis in patients with chronic hepatitis 5 and a valuable prognostic

marker of inflammation in acute pancreatitis and myocardial infarction.^[1] These results showed that RPR was regarded as an indicator of systemic inflammatory response. It was already demonstrated elevated levels of inflammatory markers, such as C-reactive protein and platelet to lymphocyte ratio to be related to poorer survival among breast cancer patients.^[6] Therefore, it was biologically feasible that RPR was a reliable prognostic indicator in breast cancer, although there have been no reports regarding the value of RPR in the prognosis of malignant disease.^[5-7]

Elevated levels of inflammatory markers, related to poorer survival among breast cancer patients RPR is regarded as an indicator of systemic inflammatory response. Elevated RPR could be an independent risk factor for prognosis in breast cancer patients. Our study demonstrated that significantly elevated RDW and RPR among elderly patients, high grade tumors and metastatic breast cancer patients. These results showed that RPR could be considered as an indicator of systemic inflammatory response in breast cancer.

There are very few studies to demonstrate that the elevated RPR could be an independent risk factor for prognosis in breast cancer patients.

Comparison With Other Studies			
Seitanides et al.	2013, Feb	Elevated RDW	-----
Takeuchi H et al.	2019, Feb	Elevated RDW	Elevated RPR (correlated with high grade tumors, metastasis and HER2 positive cases)
Present study	2019, June	Elevated RDW	Elevated RPR (correlated with high grade tumors, metastasis)

Some limitations of this study should be taken into account when interpreting the results. The analyses were performed on a small sample size, and single-centre. Potential for bias and inaccuracy in data collection as in most retrospectively studies.^[8-10]

CONCLUSION

RPR, a cost-effective and easily calculated index almost universally available using two most common haematological parameters, can improve risk evaluation. In our study the elevated preoperative RPR levels are indicative of unfavourable prognosis in patients with breast cancer. However, our results are not conclusive and should not be considered for clinical practice unless further validation due to its small sample size.

Acknowledgment

The author is thankful to Department of Pathology for providing all the facilities to carry out this work.

REFERENCES

1. Agarwal, G., Ramakant, P., Sánchez Forgach, E.R. et al. Breast cancer care in developing countries. *World J Surg*, October 2009,33:2069.
2. Chen, B., Ye, B., Zhang, J., Ying, L. & Chen, Y. RDW to platelet ratio: a novel noninvasive index for predicting hepatic fibrosis and cirrhosis in chronic hepatitis B. *PLoS ONE* 8, e68780 (2013).
3. Takeuchi H, Abe M, Takumi Y, et al. Elevated red cell distribution width to platelet count ratio predicts poor prognosis in patients with breast cancer. *Sci Rep*. 2019 Feb 28;9(1):3033.

4. Takeuchi, H. et al. The prognostic significance of the preoperative platelet-lymphocyte ratio in Japanese patients with localized breast cancer. *Adv. Breast Cancer Res.* 5, 49–57 (2016).
5. Kuniyoshi RK, et al. Gene profiling and circulating tumor cells as biomarker to prognostic of patients with locoregional breast cancer. *Tumour Biol.* 2015;36:8075–8083. doi: 10.1007/s13277-015-3529-5. [PubMed] [CrossRef] [Google Scholar]
6. Lippi G, Salvagno GL, Guidi GC. Red blood cell distribution width is significantly associated with aging and gender. *Clin. Chem. Lab. Med.* 2014;52:e197–e199. [PubMed] [Google Scholar]
7. Chen PC, et al. Red blood cell distribution width and risk of cardiovascular events and mortality in a community cohort in Taiwan. *Am. J. Epidemiol.* 2010;171:214–220. doi: 10.1093/aje/kwp360. [PubMed] [CrossRef] [Google Scholar]
8. Bojakowski K, et al. A high red blood cell distribution width predicts failure of arteriovenous fistula. *PLoS ONE.* 2012;7:e36482. doi: 10.1371/journal.pone.0036482. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
9. Chen, G. P., Huang, Y., Yang, X. & Feng, J. F. A nomogram to Predict Prognostic Value of Red Cell Distribution Width in Patients with Esophageal Cancer. *Mediators Inflamm.* 854670 (2015). [PMC free article] [PubMed]
10. Smirne C, et al. Evaluation of the red cell distribution width as a biomarker of early mortality in hepatocellular carcinoma. *Dig. Liver Dis.* 2015;47:488–494. doi: 10.1016/j.dld.2015.03.011. [PubMed] [CrossRef] [Google Scholar]