

**A study on correlation of biomarkers in gastric cancer patients to deduce cancer behaviour in a tertiary centre**

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**Abstract**

**Aim:** To correlate platelet to lymphocyte ratio, neutrophil to lymphocyte ratio as biochemical marker in deducing the behavior of gastric cancer.

**Introduction:** The platelet to lymphocyte ratio (PLR) and neutrophil to lymphocyte ratio (NLR) , reflect the systematic inflammatory response, with some evidence revealing that they are associated with poorer survival in patients with gastric cancer. Neutrophil-to-lymphocyte ratios a simple parameter which helps in predicting the outcome of the patient also tumour size, histology, nodal spread, location of tumour, have also been studied to reflect tumour behaviour and further management.

**Sample Abstract**

**Study design:** Retrospective observational study.

**Place and Duration of Study:** This study will be conducted in the Department of General Surgery, R.L. Jalappa Hospital, Kolar.

It's a retrospective study from January 2016 to December 2017 all patients diagnosed with carcinoma stomach were included in the study. The demographic data, clinicopathologic parameters, and surgical outcomes were acquired. Cancer Staging System (recent AJCC) was used for staging the tumours. Preoperative measurements of the complete blood counts and differential counts were performed 7days of admission.

**Methodology:** Data was entered using Microsoft excel and analysed using Stata version 12.0. All continuous variables such PMN count, Lymphocyte count, Platelet count, Neutrophil-Lymphocyte ratio, Platelet-Lymphocyte ratio, and Red Band width were

summarised using Mean (SD). Age categories, gender, histopathological types, and tumour site were summarised using Proportion (%). Comparison of the tumor markers across sex and age groups was done using Unpaired t-test. Comparison of the tumor markers across histopathological types and tumor site was done using Oneway ANOVA. Bar graphs and Boxplots were used to depict the categorical and continuous variables, respectively. P-value less than 0.05 were considered statistically significant.

**Results:** In the above retrospective study that was conducted in department of general surgery of R L Jalappa hospital, In 67 study subjects there was no statically significance noted in the correlation of biomarkers in gastric cancer( $p < 0.05$ ). In the present study there was no statically significant observed in the correlation of biomarkers in the gastric cancer. The supports that the antrum is most common site for gastric cancer (41- 61.2%). This study also demonstrates the utility of the RBW mean of which shows 17.9 (3.3) with mean neutrophil lymphocyte 5.3 (6.2) and lymphocyte platelet 21.5 (20.7). Rbw variation is seen more in the age group above 50years 18.3 (3.3).

**Conclusion:** A negative correlation is was found between neutrophil-lymphocytic ratios, neutrophil-platelets ratio in assessing the behavior of gastric cancer. This above mentioned ratio cannot be used to assess the aggressiveness of the tumor nor as a clinical indicator of advancement of disease. However, on comparison of RBW (Red band width) with

histological type showed that adenocarcinoma stomach has wide RBW. Study supports the fact that most common site of gastric carcinoma is antrum of the stomach 48 (71.6%) and incidence is higher in elderly male patients 16 (34.8%).

## Material and Methods

### Inclusion Criteria

1. All patient diagnosed with carcinoma stomach undergoing treatment were included in study.
2. Patients with no previous history of neoadjuvant therapy, no blood disease, no acute inflammation were included in study.

### Exclusion Criteria

1. Patients with ongoing infections, concomitant immune mediate diseases were excluded

### Statistical Analysis

Data was entered using Microsoft excel and analysed using Stata version 12.0. All continuous variables such PMN count, Lymphocyte count, Platelet count, Neutrophil-Lymphocyte ratio, Platelet-Lymphocyte ratio, and Red Band width were summarised using Mean (SD). Age categories, gender, histopathological types, and tumour site were summarised using Proportion (%). Comparison of the tumor markers across sex and age groups was done using Unpaired t-test. Comparison of the tumor markers across histopathological types and tumor site was done using One-way ANOVA. Bar graphs and Boxplots were used to depict the categorical and continuous variables, respectively. P-value less than 0.05 was considered statistically significant.

Table 1: Age and gender distribution of the study participants (n=67)

Malignancy site	Adenocarcinoma	Squamous Cell Carcinoma	Others	Total (%)
Fundus	1 (2.1%)	5 (62.5%)	0	6 (9.0%)
Body	5 (10.4%)	0	5 (45.4%)	10 (14.9%)
Antrum	34 (70.8%)	2 (25.0%)	5 (45.4%)	41 (61.2%)
Pylorus	8 (16.7%)	1 (12.5%)	1 (9.1%)	10 (15.2%)
Total	48 (71.6%)	8 (11.9%)	11 (16.4%)	

of the total participants, about two-thirds were male and more than half were aged more than 60 years. The age and the gender distribution are depicted in the figure 1.

Figure 1: Age and gender distribution of the study participants (n=67)

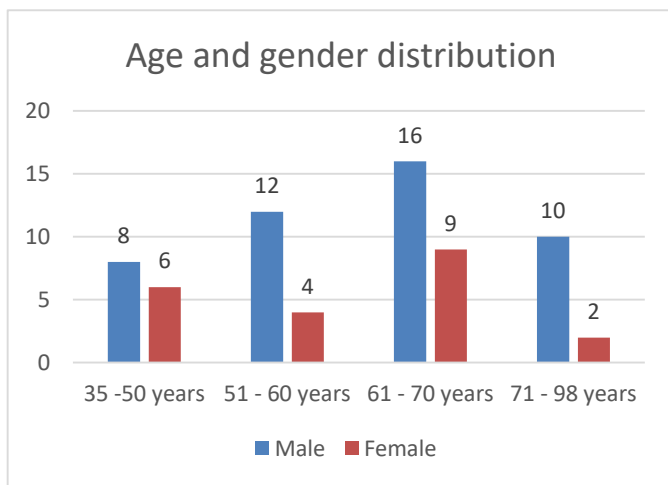


Table 2: Distribution of site and type of malignancy among the study subjects (n=67)

Age categories	Male (n=46)	Female (n=21)	Total (n=67)
36 – 50 years	8 (17.4%)	6 (28.6%)	14 (20.9%)
51 – 60 years	12 (26.1%)	4 (19.0%)	16 (23.9%)
61 – 70 years	16 (34.8%)	9 (42.9%)	25 (37.3%)
71 – 98 years	10 (21.7%)	2 (9.5%)	12 (17.9%)
Total	46 (100%)	21 (100%)	67 (100%)

Chi-square value=41.112, p-value<0.001

The commonest site of adenocarcinoma was antrum (71%) followed by pylorus (17%). Squamous cell carcinoma was common in the fundus (63%). Overall,

Adenocarcinoma was the most common type of gastric malignancy (72%). The distribution of site and type of malignancy is shown in figure-2.

Figure 2: Distribution of site and type of malignancy among the study subjects (n=67)

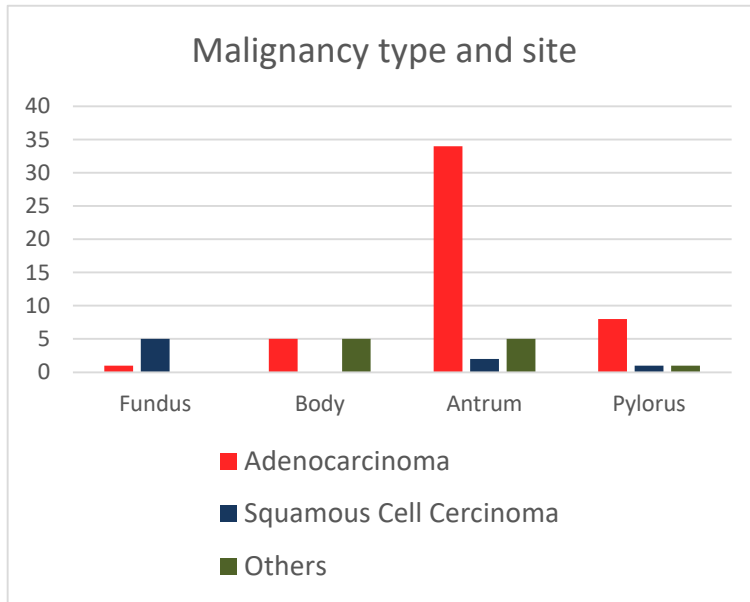


Table 3: Summary estimate of the different Biomarkers among the study subjects (n=67)

	Mean (SD)
PMN	70.9 (12.7)
Lymphocyte	20.8 (10.0)
Platelet	322.3 (129.6)
Neutrophil Lymphocyte Ratio	5.3 (6.2)
Platelet Lymphocyte Ratio	21.5 (20.7)
RBW	17.9 (3.3)

The Mean (SD) PMN % count was 70.9 (12.7) and that of lymphocyte was 20.8 (10.0). The mean (SD) platelet count was 322.3 (129.6). The mean NLR and PLR was 5.3 and 21.5 respectively. The mean RBW was 17.9 (3.3) respectively.

Table 4: Comparison of Biomarkers among the study subjects by Gender (n=67)

	Male (n=46)	Female (n=21)	p-value <sup>#</sup>
PMN	71.4 (12.9)	69.7 (12.4)	0.598
Lymphocyte	20.1 (8.9)	22.3 (12.0)	0.414
Platelet	317.4 (134.5)	333.1 (120.6)	0.649
Neutrophil Lymphocyte Ratio	4.9 (3.7)	6.2 (9.8)	0.433
Platelet Lymphocyte Ratio	19.3 (11.8)	26.4 (32.7)	0.197
RBW	18.1 (3.7)	17.7 (2.5)	0.625

**# Unpaired t-test was used to compute p-value**

The comparison of different biomarkers between male and females is shown in table 4. All biomarkers except

PMN and RBW were higher among females compared to males. However, none of the biomarkers were found to be significantly associated with the sex. Figure 4

depicts the comparison of different biomarkers between male and females.

Figure 3

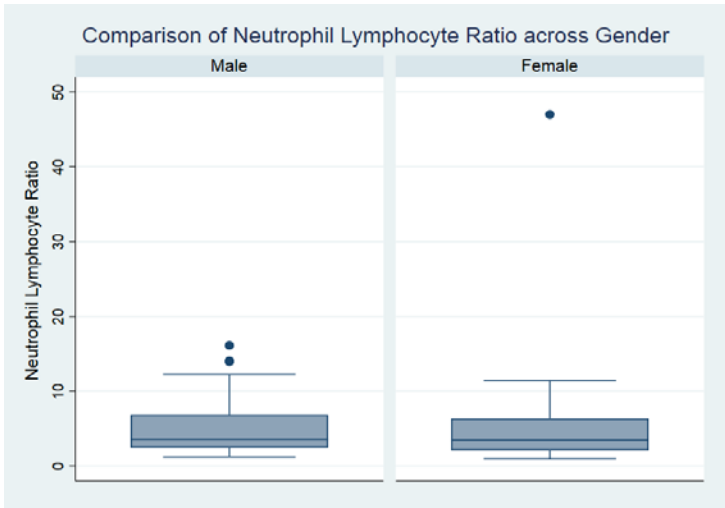


Figure 4

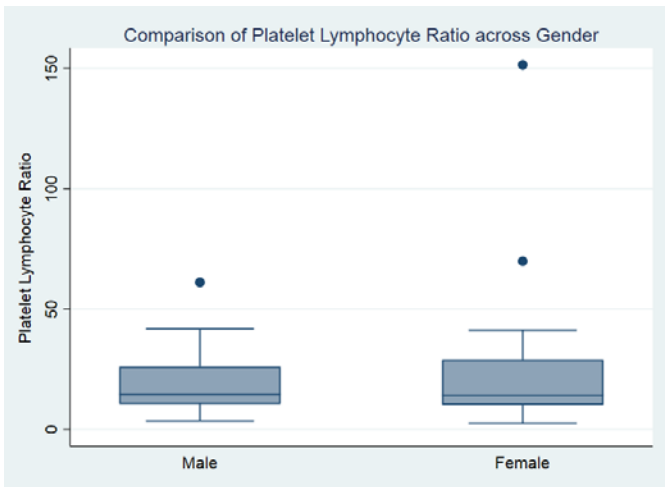


Figure 5

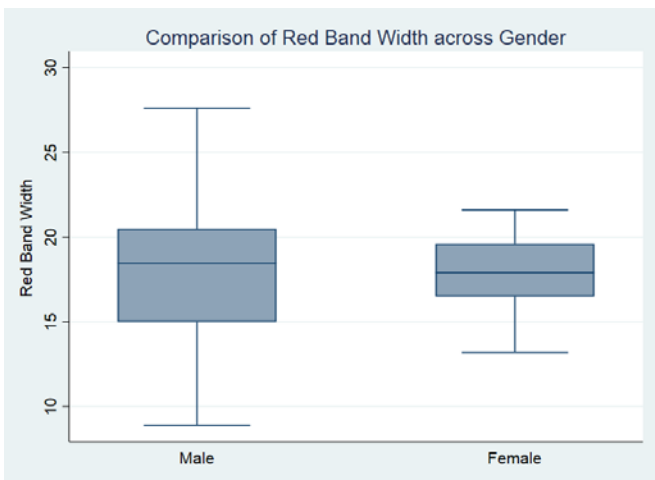


Table 5: Comparison of Biomarkers among the study subjects by age group (n=67)

	Age <=50 years (n=14)	Age >50 years (n=53)	p-value <sup>#</sup>
PMN	66.8 (14.4)	72.0 (12.1)	0.180
Lymphocyte	26.0 (9.3)	19.4 (9.7)	0.025
Platelet	305.6 (129.8)	326.8 (130.5)	0.590
Neutrophil Lymphocyte Ratio	3.27 (2.6)	5.9 (6.8)	0.162
Platelet Lymphocyte Ratio	12.8 (5.8)	23.8 (22.6)	0.078
RBW	16.6 (3.4)	18.3 (3.3)	0.078

# Unpaired t-test was used to compute p-value

The comparison of different biomarkers between two age groups (more than and less than 50) is shown in table 5. In general, elderly had higher levels of biomarkers (except lymphocyte). The mean (SD) lymphocyte % count was higher in patient less than 50

Figure 6

years and the difference was statistically significant. However, other biomarkers were not found to be significantly associated with the age group. Figure 5 depicts the comparison of different biomarkers between age groups.

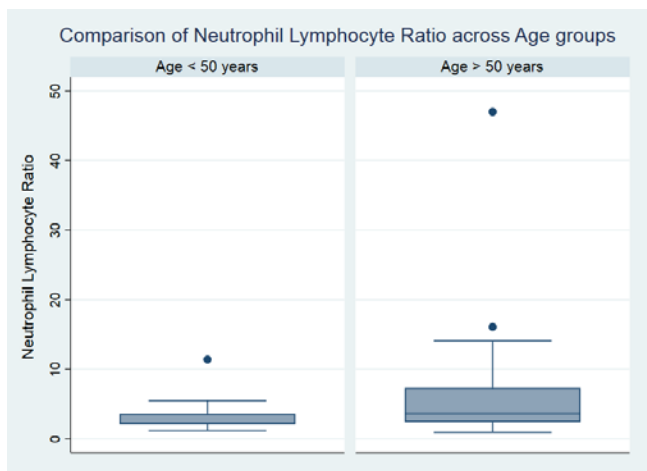


Figure 7

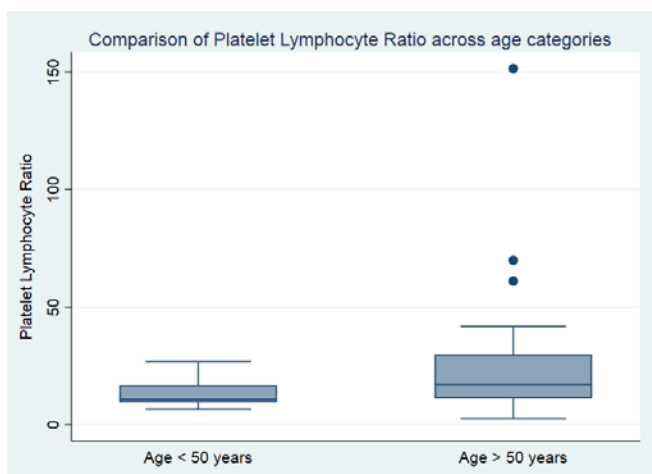


Figure 8

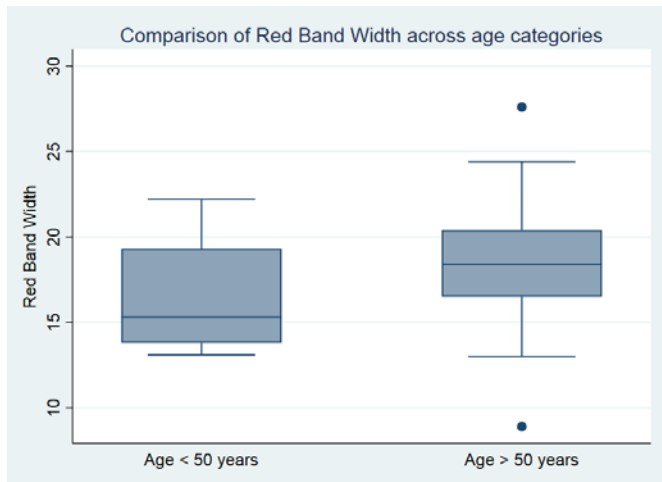


Table 6: Comparison of Biomarkers among the study subjects by histopathological type (n=67)

	Adenocarcinoma (n=48)	Squamous cell carcinoma (n=8)	Others (n=11)	p-value <sup>#</sup>
PMN	70.0 (12.9)	69.0 (14.1)	76.2 (10.3)	0.319
Lymphocyte	21.0 (10.7)	20.5 (8.8)	20.0 (7.9)	0.957
Platelet	317.2 (117.4)	308.7 (139.8)	354.5 (176.2)	0.663
Neutrophil Lymphocyte Ratio	5.6 (7.1)	4.5 (3.4)	4.9 (3.6)	0.883
Platelet Lymphocyte Ratio	22.1 (22.8)	17.5 (9.7)	21.6 (17.8)	0.848
RBW	18.0 (3.4)	16.3 (2.2)	18.8 (3.4)	0.278

# Oneway ANOVA was used to compute p-value

The comparison of different biomarkers between different types of malignancy is shown in table-6. The squamous cell carcinoma had the least value for PMN, Platelet, RBW, NLR and PLR. Lymphocyte count was

lowest for the other type of cancers. However, none of these differences observed were statistically significant. Figure 6 depicts the comparison of different biomarkers between different types of cancers.

Figure 9

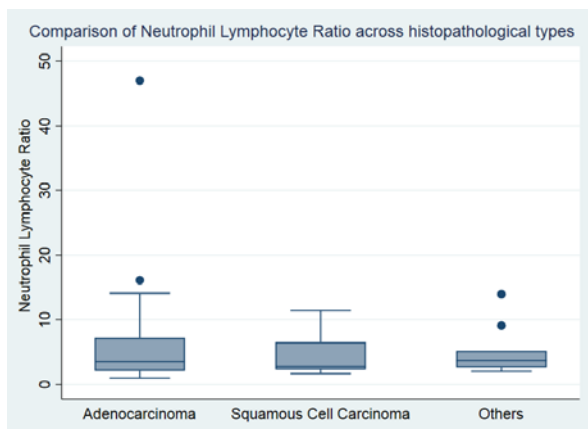


Figure 10

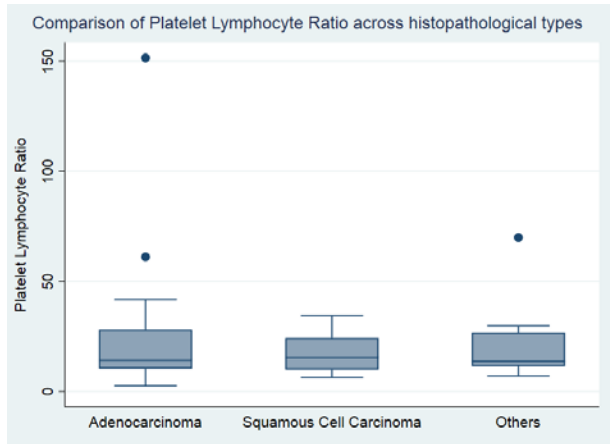


Figure 11

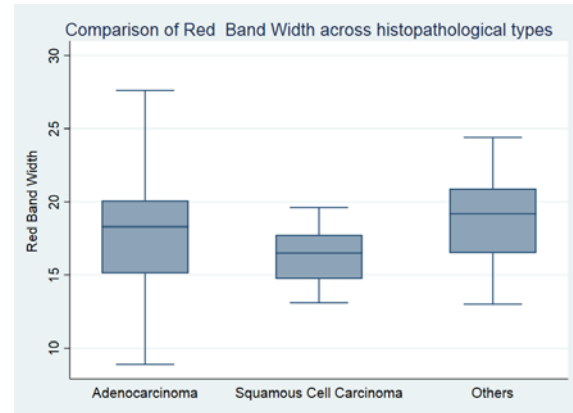


Table 7: Comparison of Biomarkers among the study subjects by site (n=67)

	Fundus (n=6)	Body (10)	Antrum (n=41)	Pylorus (n= 10)	p-value <sup>#</sup>
PMN	66.2 (14.0)	73.3 (10.3)	71.4 (12.7)	69.2 (14.8)	0.708
Lymphocyte	20.1 (9.3)	22.2 (9.5)	20.6 (10.8)	20.6 (8.7)	0.968
Platelet	280.2 (107.6)	354.9 (157.5)	328.4 (136.3)	290.4 (75.9)	0.590
Neutrophil Lymphocyte Ratio	4.50 (3.75)	4.29 (2.82)	5.89 (7.53)	4.69 (3.87)	0.852
Platelet Lymphocyte Ratio	16.08 (9.55)	21.72 (20.03)	23.14 (23.87)	17.85 (11.14)	0.814
RBW	15.9 (2.1)	17.8 (4.3)	18.6 (3.2)	16.9 (3.2)	0.201

# Oneway ANOVA was used to compute p-value

Figure 12

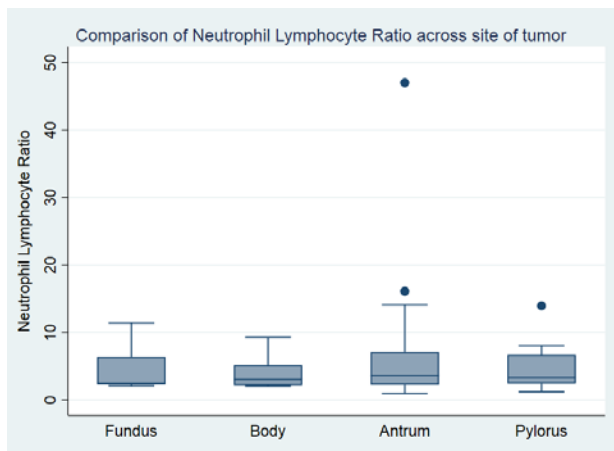


Figure 13

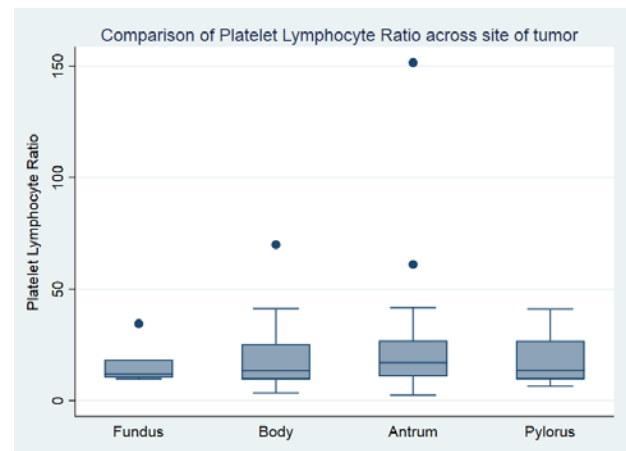
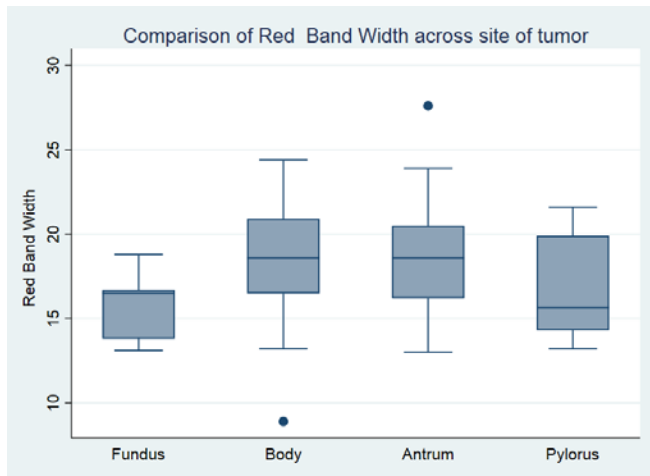




Figure 14



### Results And Discussion

In the above retrospective study that was conducted in department of general surgery of R L Jalappa hospital, In 67 study subjects there was no statically significance noted in the correlation of biomarkers in gastric cancer( $p < 0.05$ ). In the present study there was no statically significant observed in the correlation of biomarkers in the gastric cancer. The supports that the antrum is most common site for gastric cancer(41-61.2%). This study also demonstrates the utility of the RBW mean of which shows 17.9 (3.3) with mean neutrophil lymphocyte 5.3 (6.2) and lymphocyte platelet 21.5 (20.7). Rbw variation is seen more in the age group above 50years 18.3 (3.3). However, on comparison of RBW (Red band width) with histological type showed that adenocarcinoma stomach has wide RBW. Study supports the fact that most common site of gastric carcinoma is antrum of the stomach 48 (71.6%) and incidence is higher in elderly male patients 16 (34.8%). It is a study done in a single tertiary centre, hence study needs more data and multicentric analysis to conclude. The prognostic role

can not be commented upon since the study is retrospective.

### Conclusion

A negative correlation is was found between neutrophil-lymphocytic ratio, neutrophil-platelets ratio in assessing the behavior of gastric cancer. This above mentioned ratio cannot be used to assess the aggressiveness of the tumor nor as a clinical indicator of advancement of disease. However, on comparison of RBW (Red band width) with histological type showed that adenocarcinoma stomach has wide RBW. Study supports the fact that most common site of gastric carcinoma is Antrum of the stomach 48 (71.6%) and incidence is higher in elderly male patients 16 (34.8%).

### References

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65:87–108.
2. Colotta F, Allavena P, Sica A, et al. Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability. Carcinogenesis. 2009; 30: 1073–1081.

3. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*. 2011;144:646–674.
4. Zou W. Immunosuppressive networks in the tumour environment and their therapeutic relevance. *Nat Rev Cancer*. 2005; 5: 263.
5. Roxburgh CS, McMillan DC. Role of systemic inflammatory response in predicting survival in patients with primary operable cancer. *Future Oncol*. 2010;6:149–163.
6. Aizawa M, Gotohda N, Takahashi S, et al. Predictive value of baseline neutrophil/lymphocyte ratio for T4 disease in wall-penetrating gastric cancer. *World J Surg*. 2011;35:2717–2722. doi: 10.1007/s00268-011-1269-2.
7. Jung MR, Park YK, Jeong O, et al. Elevated preoperative neutrophil to lymphocyte ratio predicts poor survival following resection in late stage gastric cancer. *J Surg Oncol*. 2011;104:504–510.
8. Ubukata H, Motohashi G, Tabuchi T, et al. Evaluations of interferon- $\gamma$ /interleukin-4 ratio and neutrophil/lymphocyte ratio as prognostic indicators in gastric cancer patients. *J Surg Oncol*. 2010;102:742–747.
9. Zhang Y, Lu J-J, Du Y-P, et al. Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in gastric cancer. *Medicine (Baltimore)* 2018;97:e0144.
10. Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. *J Clin Epidemiol* 2003;56:1-9.
11. Andreyev HJ, Norman AR, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer* 1998;34:503-509.
12. Lochhead P, El-Omar EM. Gastric cancer. *Br Med Bull* 2008;85:87-100.
13. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2002;55:74-108.
14. Wang FEN, Liu ZY, Xia YY, Zhou C, Shen XM, Li XL, et al. Changes in neutrophil/ lymphocyte and platelet/lymphocyte ratios after chemotherapy correlate with chemotherapy response and prediction of prognosis in patients with unresectable gastric cancer. *Oncol Lett* 2015;10:3411e8.