

Hematological Inflammatory Parameters: Can They Play a Role as Cancer Biomarkers?

Anu Agarwal¹, Hiral², Mukta Pujani³, Sujata Raychaudhuri⁴, Charu Agarwal⁴, Akanksha Bajaj¹, Reetika Menia¹

¹Tutor, ²MBBS Student, ³Associate Professor, ⁴Assistant Professor,
Department of Pathology, ESIC Medical College and Hospital, Faridabad, Haryana

Corresponding Author: Anu Agarwal

ABSTRACT

Background: Cancer is one of the most important causes of morbidity and mortality worldwide. Association of cancer with systemic inflammation has been widely established. A complete blood count may reveal changes in cell lines as a result of inflammation.

Method: The study was conducted in the Department of Pathology at ESIC Medical College, Faridabad in duration of 3 months (July 2018- September 2018). A total of 30 cancer cases and 30 controls were included in the study. The haematological parameters (neutrophil, lymphocyte, monocyte count and platelet count) and indices (NLR, PLR and LMR) were evaluated and statistical analysis was done to find a relationship between the above mentioned indices and cancer.

Result: According to our study NLR and PLR along with absolute neutrophil count and platelet count showed a significant difference between cancer cases and controls. However, there was no significant difference between cancer and control groups in terms of LMR values.

Conclusion: Absolute neutrophil and platelet count alongwith NLR and PLR can be used as markers of systemic inflammation in cancer

Key Words: cancer, systemic inflammation, haematological indices

INTRODUCTION

Cancer is one of the leading causes of death worldwide and is responsible for an estimated 9.6 million deaths annually. Globally, about 1 in 6 deaths is attributed to cancer leading to approximately 70% of deaths. [1] It is now widely recognised that patient outcome with cancer is not only determined by tumour characteristics alone but also the host related factors are also important. In the last decade, it has become increasingly apparent that cancer-associated inflammation is a key determinant of disease progression and survival. [2,3] It is also well established that the systemic inflammatory response is associated with alterations in circulating white blood cells. [4,5] Haematological tests are carried out routinely for cancer patients in a variety of clinical scenarios, and as such represent an easily measurable objective parameter able to express the severity of the systemic

inflammatory response in patients with cancer.

The individual blood cell parameters are easily fluctuated by dehydration/overhydration, diluted blood specimens and blood specimen handling. Hence, to study the interaction between blood cells, various stable indices have been derived such as NLR (neutrophil to lymphocyte ratio), PLR (platelet to lymphocyte ratio) and LMR (lymphocyte to monocyte ratio). A High NLR and PLR; and Low LMR have been linked to malignancy and poorer prognosis of cancer patients. [6-8]

Considering the importance of inflammatory pathways in cancer development we designed this study to evaluate hematological parameters (NLR, PLR, LMR) in different types of malignancies and to analyse whether these hematological parameters are useful markers to differentiate between cancer

patients and healthy individuals by determining the level of NLR, PLR and LMR particularly.

MATERIAL AND METHODS

This was a prospective case control study conducted in the Department of Pathology, ESIC Medical College and Hospital, Faridabad over a 3 months period from July 2018 to September 2018. Approval was obtained from institutional ethics committee and consent was taken from all patients.

The study comprised of 30 cases of solid organ malignancies with established pathological diagnosis and 30 age and gender matched healthy controls. Patients with history of cardiovascular disease, metabolic syndromes, inflammatory bowel disease, haematological disorders, kidney or liver disease and any other disease that might alter the haematological parameters and patients on anti-platelet medication were excluded from the study.

Venous blood samples were collected in aseptic conditions in the EDTA vacutainer. Samples were run on automated counter Sysmex XN1000 and the haematological findings like absolute neutrophil count, absolute lymphocyte count, absolute monocyte count and platelet count were noted. Subsequently, NLR (Neutrophil to Lymphocyte ratio), PLR (Platelet to Lymphocyte ratio) and LMR (Lymphocyte to Monocyte ratio) were calculated.

Statistical Analysis- The mean and standard deviation of all the parameters were calculated in cases and controls. A comparison in haematological indices between the cases and controls was done using t test and p value <0.05 was considered to be significant.

OBSERVATIONS AND RESULTS

A total 30 cases with a pathological diagnosis of cancer and 30 controls were included in the present study. The patients in both the groups were in the age of 20 to 70 yrs. The mean age of the cases was 50

years with most of the patients in the age group 41-50yrs (36.7%) (Figure 1). Most of the patients were males, contributing 70% of the cases (Figure 2). As seen in Table 1, the most common solid organ malignancy was SCC oral cavity comprising of 36.7% of the cases followed by SCC larynx. Also, most of such patients were males (8 out of total 11 cases). Table 2 depicts the difference in mean of various haematological parameters in cancer cases versus control patients.

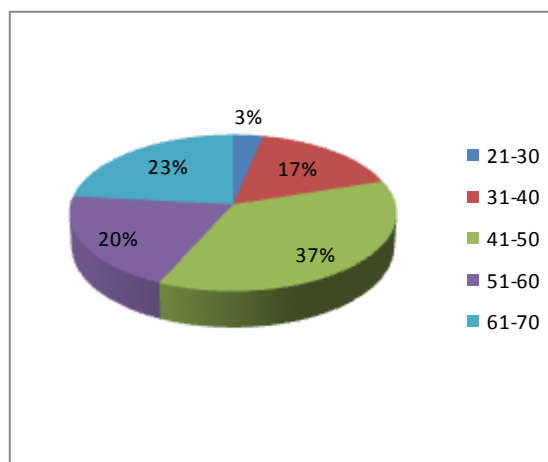


FIGURE 1: AGE-DISTRIBUTION OF CASES

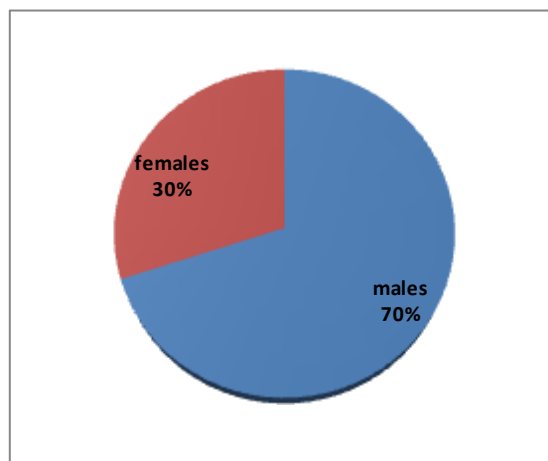


FIGURE 2: GENDER-DISTRIBUTION OF CASES

TABLE 1: DISTRIBUTION OF CASES ACCORDING TO DIAGNOSIS

Diagnosis	No. of cases (n=30)
Squamous Cell Carcinoma Oral cavity	11
Squamous Cell Carcinoma Larynx	6
Adenocarcinoma Oesophagus	1
Carcinoma Cervix	4
Carcinoma breast	5
Carcinoma prostate	1
Carcinoma Thyroid	2

This difference was statistically significant in terms of absolute neutrophil count, platelet count, NLR and PLR. The mean NLR in cancer cases and controls was 3.02 ± 1.45 SD and 1.77 ± 0.41 SD respectively. As evident from Figure 3, in most of the cases NLR was higher in cancer patients as compared to controls. Also, the

difference between these was statistically significant, $p < 0.0001$. Mean PLR was also higher in cancer cases versus controls (161.50 ± 60.66 SD vs 112.35 ± 37.04 SD) (Figure 4). Similar to NLR, the difference in PLR between cancer cases and controls was statistically significant, $p = 0.0004$.

TABLE 2: COMPARISON OF HAEMATOLOGICAL INDICES IN CANCER AND CONTROL PATIENTS

Hematological index	Cancer cases (mean+ SD)	Controls (mean+ SD)	P value
Absolute neutrophil count ($\times 10^3/\text{cumm}$)	5.64+-2.18	3.57+-0.78	<0.0001
Absolute lymphocyte count ($\times 10^3/\text{cumm}$)	2.03+-0.74	2.06+-0.52	0.8530
Absolute monocyte count ($\times 10^3/\text{cumm}$)	0.69+-0.34	0.64+-0.36	0.6095
Platelet count ($\times 10^3/\text{cumm}$)	312.7+- 22.15	225.96+- 13.56	0.0015
NLR	3.02+-1.45	1.77+-0.41	<0.0001
PLR	161.50+- 60.66	112.35+- 37.04	0.0004
LMR	4.42+-5.94	3.71+- 1.52	0.5845

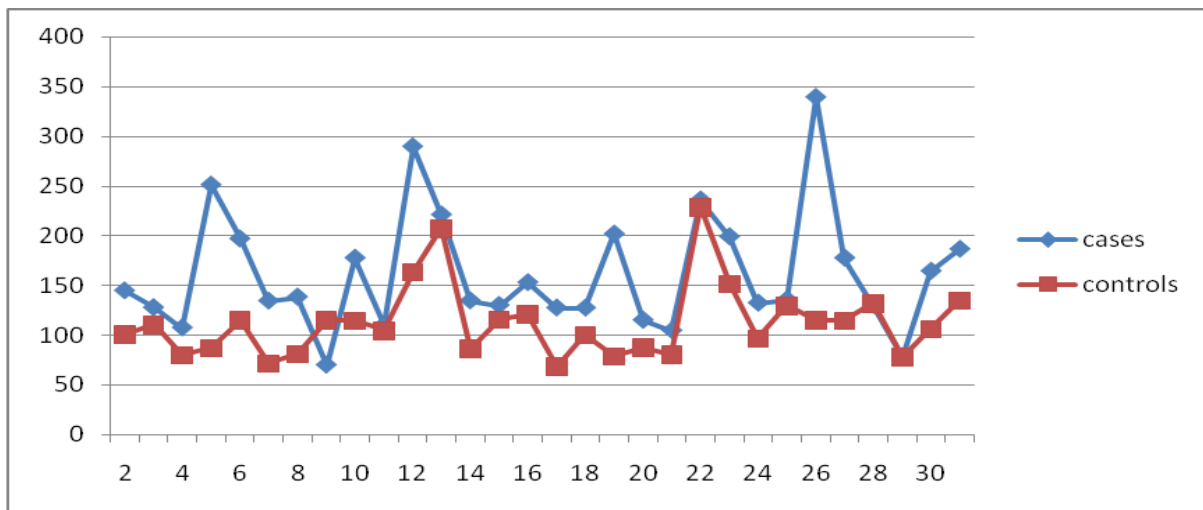


FIGURE 3: NLR IN CANCER CASES AND CONTROLS

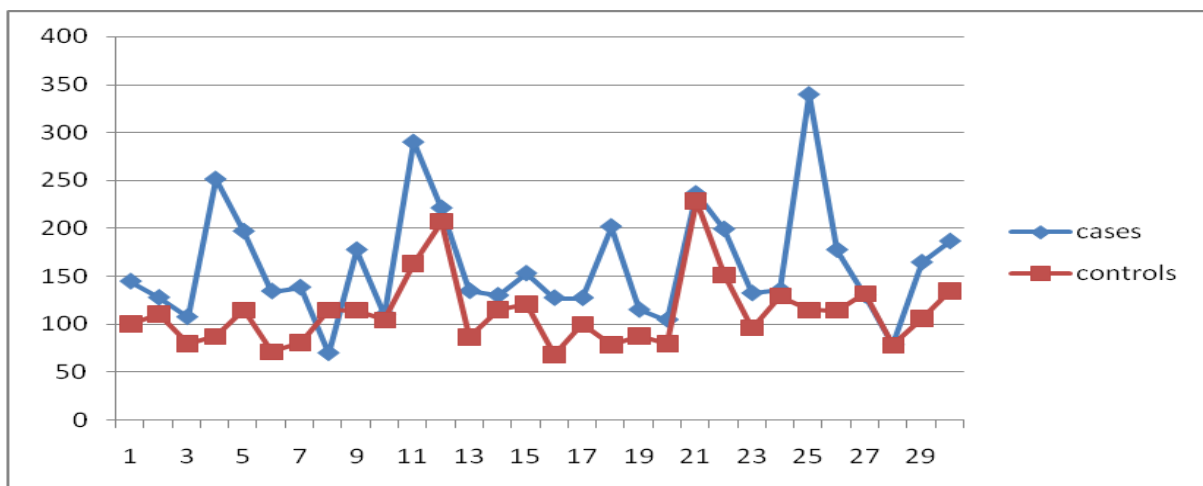


FIGURE 4: PLR IN CANCER CASES AND CONTROLS

DISCUSSION

The relationship between inflammation and cancer development is

one of the most investigated issues in the last decade. [9] In this study there was a significant increase in absolute neutrophil

count in cancer cases as compared to their age and gender matched controls ($p < 0.0001$). It increased from $3.57 (\pm 0.78) \times 10^3$ per cumm to $5.64 (\pm 2.18) \times 10^3$ per cumm. Similar increase was found by Grimm et al [10] when they compared haematological parameters among oral squamous cell carcinoma and controls and found that absolute neutrophil count increased from $4.67 (4.34-5.00) \times 10^3$ per cumm to $5.68 (5.33-6.02) \times 10^3$ per cumm with a $p < 0.0001$. However, in a study conducted by Duzlu et al, [11] the difference between malignant, benign and control groups was not statistically significant ($p = 0.020$).

Our study also showed a significant change in platelet count when observed in cancer cases versus controls. It increased from $225.96 (\pm 13.56) \times 10^3$ per cumm to $312.7 (\pm 22.15) \times 10^3$ per cumm. $p = 0.0015$. A similar increase was observed by Duzlu et al [11] and Grimm et al [10] but the difference was not statistically significant. (p value of 0.8360 and 0.950 respectively).

Absolute monocyte count has also been studied by various authors. [12-15]

However, absolute monocyte count mainly has a role as a prognostic marker in various malignancies. The prognostic value of monocyte has been reported not only in lymphomas, but also in solid tumours. [9,16] Increase of circulating monocyte was associated with poor survival and outcome in non-small cell lung cancer, gynecological cancer, and gastrointestinal cancer. [16-18] In our study, the difference in absolute monocyte count between cancer cases and controls was not significant, $p = 0.6095$.

A low lymphocyte count has been frequently observed in advanced cancer patients. It has also been found to be associated with poor overall survival in patients with various types of cancer. [19,20] We compared absolute lymphocyte levels in cancer patients and their respective controls and did not observe any significant change, $p = 0.8530$. However, Duzlu et al [11] and Grimm et al [10] found a significant decrease in lymphocyte count in oral cancer patients

as compared to their respective controls ($p < 0.0001$).

In addition to studying the individual haematological parameters, it is also important to study their interactions. For this we derived NLR (neutrophil to lymphocyte ratio), PLR (platelet to lymphocyte ratio) and LMR (lymphocyte to monocyte ratio).

In our study, NLR increased significantly from 1.77 ± 0.41 in controls to 3.02 ± 1.45 in cancer patients ($p < 0.0001$). This was in concordance with the findings of Duzlu et al [11] ($p < 0.001$) and Grimm et al [10] ($p < 0.0001$) oral cancer, Kemal et al [21] ($p < .001$) and Bednarska et al [22] ($p < 0.0001$) in ovarian cancer, and Pietrzyk et al [23] ($p = 0.020$) in gastric cancer.

Similar to NLR, the increase in PLR was also significant in our study. It was observed that there was an increase in value of PLR from 112.35 ± 37.04 in controls to 161.50 ± 60.66 in cancer cases. Also this difference was statistically significant ($p = 0.0004$). These results were similar to the findings of Kemal et al [21] and Ozaksit et al [24] ($p < .001$ and $p = .004$ respectively) in ovarian cancer patients. Also, Pietrzyk et al [23] in gastric cancer patients found a similar significant increase in PLR ($p = 0.002$). Grimm et al [10] also found that PLR values increase significantly in oral cancer ($p = 0.001$).

In contrast to NLR and PLR, our study revealed that LMR values did not change significantly in cancer cases with respect to controls ($p = 0.5845$). However, Grimm et al [10] in their study observed a significant decrease in LMR from $5.43 (5.01-5.84)$ in controls to $3.57 (3.30-3.83)$ in cancer patients.

Hence, according to our study haematological indices namely absolute neutrophil count and platelet count along with NLR and PLR can be used as reliable markers of detection of cancer.

Limitations

The limitations of the study include a small sample size as the duration of the

study was only for a short period of 3 months. In addition we could not compare the difference in haematological parameters among cancer of different sites due to small sample size leading to uneven distribution of cases. Also, the lack of serial evaluation of the abovementioned parameters throughout the course of disease was another drawback which is necessary in order to comment upon their value as prognostic markers in addition to being markers of detection. Hence, this study can be used as pilot project for further studies in future.

CONCLUSION

Cancer is one of the most important causes of morbidity and mortality worldwide. According to our study, absolute neutrophil count and platelet count increase significantly in cancer. Also, NLR and PLR can reliably be used as markers for detection of cancer. However, in our study there were no significant changes in LMR in cancer patients. Thus, the haematological indices mainly NLR and PLR are easily available and cost effective tools that can be used for

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